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# PLASTIC PLEURISY IN INFANCY*

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## ETIOLOGY

The time has passed when the subject of pulmonary and pleuropulmonary congestions was a live controversy, and when extensive reports were devoted to the description of the condition. The old text of Cadet de Gassicourt devotes forty-eight pages to this subject and gives an admirable clinical description.

In the older literature, this condition was described under many different terms, such as simply pulmonary congestion (Woillez), splenopneumonia (Grancher), pleuropulmonary congestion (Potain) and inflammation of the chest (Dupre and Dieulafoy). All these terms really meant the same thing, and none of this old terminology is now used. The terminology of the French pediatricians, Besancon and de Jong, is the one now adopted. The pathologic concept of pulmonary congestions is now fully understood. All so-called pulmonary and pleuropulmonary congestions are called broncho-alveolitis and cortico-pleuritis. In this manner the proper definition defines both as a clinical entity. The terminology itself implies the ordinarily fleeting, ephemeral character of the disease. It is well known, however, that many of these so-called pulmonary or pleuropulmonary congestions are prolonged, and often leave the patient's recovery in doubt. It is clear, however, that an exact and simple nomenclature is indispensable for the comprehension of the clinical facts.

In the classification of Besancon and de Jong, there is only one type of acute pulmonary congestion, as observed in certain intoxications (with alcohol, absinth, hydrocyanic acid), in snake-bite poisoning, in eclampsia, in diabetes, in heat stroke or cold shock. There is in these conditions a truly acute congestion and pulmonary edema.

In the pathologico-anatomic studies we have found more or less generalized hyperemic lesions with true pulmonary hemorrhage. No

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other lesions except those of these types are found. On account of the suddenness of its action and the necropsy observations, the term congestion is justified. The old pulmonary and pleuropulmonary congestions must therefore be classified as belonging to one of three types; namely, pulmonary congestion proper, acute broncho-alveolitis and plastic pleuritis. Acute broncho-alveolitis is really nothing more than aborted pneumonia or bronchopneumonia arrested in the period of engorgement. Our observations on the sputum agree with those of Besancon and de Jong, who have shown the cytologic and histologic identity of this condition with a beginning pneumonia.

In the evolution of generalized infections (typhoid, grip, rheumatism, etc.), localization in the lungs may take place. The older writers called this delayed or secondary pulmonary congestion.

In another class of cases still different from these, broncho-alveolitis presents itself as a complication of conditions already localized in the respiratory tract. This form is particularly frequent in early childhood and is a common experience in pediatric practice.

## SYMPTOMS

The nursing infant, during the first few days of the disease, presents a rhinopharyngitis. This is followed by coryza, redness of the throat, dry cough, and fever. The infection remains so localized in the beginning. Pulmonary auscultation is negative. There are no râles and no other sounds which indicate the participation of the lower segments of the bronchial tree in the disease process at this period. Everything can be arrested at this stage in a comparatively short time. Again, the process will last longer, particularly if the infant has a lymphatic constitution, with large tonsils and adenoid hypertrophy, in which foci of infection persist and continually flare up.

Often, however, the infection descends the respiratory tract. Coarse bronchial sounds are heard on auscultation. Somewhat later, foci of fine râles appear. Their location may vary, but they are commonly found in one or both bases. The fine râles at the focus are the fundamental characteristic. There is lessened resonance to percussion over the foci; coarse or soft tubular breathing is heard, and the transmitted sobbing of the infant may be heard over the affected area. A broncho-alveolitis is established. It is worthy of note that in the descent of the infection the larynx escapes, or, if it is involved, it is in so slight a degree that there is hardly any clinical evidence. At times, the broncho-alveolitis breaks out as an acute flare-up in the course of a chronic bronchitis. In infancy this is particularly frequent, affecting the old pulmonary foci of infection.

In the subject with pulmonary tuberculosis, a focus of alveolitis may develop. Besancon and de Jong state that a tuberculous patient who has

not yet been placed at rest nor has received the hygienic and dietetic treatment will develop an extensive focus of moist râles. Sabowin has advanced the opinion that these are râles of obstruction or of fatigue. After the râles have disappeared, abnormal breathing is observed. Other types of râles may appear, but generally much less extensively than the first. A third possible sequel of these acute pulmonary congestions is seen in the formation of a plastic pleurisy. This is the pleuropulmonary congestion referred to by older writers. In this condition, the peripheral alveoli of the lungs are really involved more than is the adjacent pleura, although the anatomic and topographic term would indicate that this structure is primarily attacked. Based on structural and clinical aspects, plastic pleurisy may either be fleeting or of a persistently protracted type. The former is characterized by its mild, transient attack, the brief and quickly disappearing character of the symptoms, and the absence of any pronounced functional signs. The protracted forms correspond to the picture which Grancher drew, in 1883, under the term splenopneumonia. These protracted cases are of long duration. Conspicuous among the symptoms common to all forms must be mentioned the fundamental characteristic of the râles. These rapidly become moist and bubbling so markedly that they may even give the impression of a localized focus of softening and may even resemble a small cavity. The symptomatology of the plastic pleurisy syndrome is physical and functional. Both classes of symptoms have a brusk beginning. Particularly in infancy, these conditions begin with acute violent reactions almost stormy in character. Fortunately, however, these disappear rapidly in most cases. The "stitch" in the side, more or less intense or sustained, with which an attack is usually initiated, is generally absent in the small infant. In older children it is observed (cases 3, 4, 5 and 6). Deep percussion shows diminution of resonance and dulness of varying degree. The most frequent seat of the lesion is found posteriorly and in the middle and inferior part of the lung. The dulness may, however, extend to other areas and is often distinct over the interlobular fissures. It is the characteristic dulness found over interlobular effusions. Cases 3 and 9 illustrate this condition. Both were protracted types. The dulness was so pronounced that exploratory puncture was made, with negative results in both instances.

### DIFFERENTIAL DIAGNOSIS

A helpful point in the differential diagnosis of a doubtful case is the presence of resonance in the space of Traube. It is always present in plastic pleurisy and generally absent in effusion. Slight transitory effusions can occur in plastic pleurisy.

In some private cases, not included in this report, we have found a few cubic centimeters of turbid liquid in which polymorphonuclear cells predominated. The effusion may be pronounced, but is never so exten-

sive as in true pleural exudates. Careful examination of any fluid which may have been obtained is of value in determining the possible cause of the disorder. Predominance of lymphocytes is favorable, although one more generally finds a relative increase of polymorphonuclear cells. Bacteriologic examination of the fluid, and particularly the inoculation of a guinea-pig with it, will give valuable information.

The presence or absence of vocal fremitus is of no particular importance in the differential diagnosis between plastic pleurisy and effusion. This is illustrated in cases 2 and 3. Pleural exudate may almost certainly be excluded. Nevertheless, the vocal fremitus was scarcely perceptible.

Auscultation gives moderately valuable information. The small infant who develops pleurisy in the course of a descending infection of the bronchial tree will show a focus of fine râles over one or both bases of the lung. To hear and to differentiate these, it is necessary to auscultate the nursling habitually. Often the râles cannot be heard because the infant breathes so superficially, but they may usually be discovered if one waits for the occasional deep inspiration which the sick infant will take. The râles will not always remain in a circumscribed focus. They may at times be heard over extensive pulmonary areas (case 2). Unmistakable friction rubs may accompany these râles, which may vary as to location and the time when they appear. In some cases, the appearance of râles may be early; in others, they are absent at the beginning and only make their appearance at the decline of the infection; or again all the signs are heard at the beginning of the disease, and then presently disappear. The entire physical picture otherwise remains (dulness, bronchial breathing and diminished breath sounds). It is the picture of the splenopneumonia described by Grancher.

We have said that râles in the grave form take on a moist bubbling character, giving the impression of a localized softened area, or a lesion similar to a small cavity. The breath sounds form a valuable but rather variable semiological factor of plastic pleurisy. All that has been said about the variability of the râles is also applicable to the breath sounds. Their acoustic characteristics are variable. There are veiled breath sounds, distant sounds, peculiar expiratory sounds, and such tubular breathing as is heard in various stages of pneumonia. Frequently breath sounds are called pleural, on account of their partly tubular, partly pleural, character. Whatever their pitch, distribution and intensity, that which habitually characterizes these sounds is their variation. They are never the same at any given moment. There are exceptions to this rule, as shown by case 3. This patient showed double breath sounds over the left lower thorax, which continued for more than a month with little variation.

Characteristic voice changes such as egophony, bronchophony and subdued pectoriloquy are heard at times (cases 2, 3 and 4).

Accentuated retraction of the left side of the thorax, with dorsal and lateral scoliosis, was observed in case 3. All these manifestations disappeared during convalescence.

The temperature, as in all acute infections, rises abruptly. While it generally continues high, its duration and intensity depend on the course of the infection. At times, one sees it fall in a brisk crisis. In some cases, it is not much elevated. In other cases it shows periodic rises which signalize the lighting up of the original foci or the development of new ones. In the protracted forms the usual termination is by lysis. It is often difficult to determine what actually brings about the abrupt and spontaneous fall of the temperature. Whether it is the result of remedies used, or whether vaccine treatment, of late so much in vogue, can accomplish it, is doubtful. Based on a large and varied experience in our service with this form of therapy, we cannot share the enthusiasm of its numerous adherents. We have the impression that much more vaccine than is necessary is injected. We can definitely state that in the protracted types, the injection of polyvalent vaccine is without effect and that the fleeting transitory forms take about the same course with or without the use of vaccines.

The cough, of varying degree, which generally accompanies the process, may be dry at the beginning. In some cases it persists throughout the entire course of the disease. Older children have expectoration. This varies in microscopic appearance. It may be mucus or mucopurulent, or it may be gelatinous and adherent, or even rusty in quality. Histologic and chemical examinations, reported by Besancon and de Jong, showed the characteristic sputum of aveolitis, an albuminous exudate and alveolar cells.

The examination of the sputum is of value in determining the etiology of this condition. The bacillus of Koch must always be searched for both by direct examination and by animal inoculation.

Dyspnea may develop. This is particularly true in the small child. We have not encountered it in many of our cases. Its appearance justifies alarm and should cause grave apprehension.

There may be profound and prolonged prostration, with marked pallor. This is heightened by slight cyanosis of the lips, cheeks and ears. The alae nasi are continually distended. The child seems to have lost all strength. Fortunately, this picture does not continue long in the majority of cases, and there is often, even in a few hours, a rapid turn for the better.

To differentiate between broncho-alveolitis, with or without pleural participation, and the various anatomic stages of a classic bronchopneumonia, is difficult if not impossible. The progressive and charac-

teristic development is the factor which, above all, establishes the diagnosis. The transitory physical and functional symptoms in the one and the grave severe symptoms and prolonged course in the other are suggestive. The roentgenogram generally shows very little. There may be some shadows corresponding to localization of the process at a given point. The intensity of the shadow depends on the degree of lung and pleural involvement.

The etiology of this process which one may regard as primary, even though it may occur in the course of an already established infectious process (rheumatism, typhoid fever, etc.), is generally pneumococcic or tuberculous. From a practical standpoint, a categorical differentiation is not easy. Although the duration of the process is a valuable criterion, it cannot serve as an absolutely certain differential test. It is apparent that the transitory forms will give less suspicion of a bacillary infection than the protracted forms, but one must not consider this as axiomatic. In cases of short duration, the forms may be tuberculous. Besancon and de Jong explain them as a phenomenon of supersensibility to pulmonary allergy. They believe that in latent tuberculosis the bacilli are at liberty. Under various provocative causes (chilling, overfeeding, infectious diseases), they may form a localized focus. The mobilization of these bacilli, lodged in old, partially healed or sclerosed lung areas, provokes acute processes which may be more or less extensive or may be purely superficial.

Prolonged, protracted forms, on the other hand, may not be tuberculous. Proof of this is given in case 2, in which the process lasted one and one-half months. Tuberculosis could be ruled out both on the part of its antecedents and because of the absolutely negative results of five tuberculin injections given in increasing dosage.

In small children, the cause is practically never found in tuberculosis. At this age the infection is much more severe than it is in the simple, more or less transitory, pulmonary or pleuropulmonary processes of older children. We are convinced that in the infant, at this period, either influenza or grip, in its customary forms, is a much more common cause. Experience with the familiar attack of grip shows clearly the predominance of this infection during the winter. It begins with coryza and redness of the pharynx. The process descends the bronchial tree progressively. Tuberculosis is generally absent in the environment. A cure is definitely effected without any bad after-effects. As the patient advances in age, tuberculosis must be borne in mind more. Even so, it is still much less frequent than in the adult. The differential characteristics between the tuberculous forms and the pnuemococcic are many. They can be divided into conjectural and positive signs. These have

been well stated by Drs. Mortini and Gonada in the treatise on this subject. We quote their remarks, adding some additional signs of particular value and significance noted in infancy.

ETIOLOGY

*Conjectural and Positive Signs*

| *Tuberculous Form* | *Pneumonic Form* |
|---|---|
| Previous asthenia | Develops in a sound organism |
| Debilitating factors | Absence of these |
| Tuberculous antecedents | Negative antecedents |
| No appearance of herpes | Herpes possible |
| Localization in apexes and interlobular spaces | Usually over the bases of lungs |
| Prolonged development and tendency to relapse | Development and cyclic tendency |
| Inoculation of pleural fluid giving positive result | Negative inoculation |
| Confirmatory proof of presence of Koch bacillus in sputum, direct examination and inoculation | Negative |
| Tuberculin reaction, Pirquet and Mantoux + + | Repeated tests negative |
| Other concomitant tuberculous lesions (osseous, glandular, etc.) | Absence of these |

The familiar time-honored therapy is particularly effective in cases in which there is no tuberculous infection. Local and general counter irritation (by packs, cataplasms, warm baths, with mustard, if there is threatened collapse) is always indicated. Expectorants are good; also nasopharyngeal disinfection and the use of epinephrine. Attention to general hygienic measures, such as suitable room temperature, especially during the winter months, and proper ventilation, are essential details of a proper and sensible care of the patient. They will be effective in the majority of instances. The more serious cases respond at times to colloidal therapy or to antipneumococcic serum. We are not convinced of the efficacy of vaccine therapy in this condition.

CASE REPORTS

CASE 1.—*History.*—E. F., a boy, aged 5 years, an Argentinian, was admitted to the hospital, March 27, 1924. His parents were well; his mother had had no abortions. There were six other children, all of whom were well. This child had not had the usual infections of childhood.

Chilliness and some cough had been present for five days prior to examination. There had been no elevation of temperature or other pronounced symptoms. Two days before admission the child drank kerosene. The cough seemed more severe following this. Some fever and dyspnea also developed.

*Physical Examination.*—The child showed the development usual for his age. There was good panniculus adiposus. The skin and mucosae had a good color. There were impetiginous lesions near the nasal orifices. Over the left parieto-occipital region there was a cicatrix with alopecia (result of a burn). There was accentuated dyspnea, with distention of the alae nasi. The cough was catarrhal

in type. Moist râles could be heard faintly over the posterior part of both lungs. Both bases of the lung, but particularly of the right, showed slight areas of dulness. Auscultation, from the apex of the lung down toward the base, showed numerous sibilant râles. Over the areas of dulness, in both bases, a focus of fine crepitant râles was heard. The respiration over these areas was harsh and tubular. Percussion of the anterior part of the lung and the axillary regions was negative, but auscultation revealed sibilant râles. The cardiac dulness showed normal limits. Both heart sounds were normal. The pulse was regular (about 140 beats to the minute), and showed good volume. The abdomen showed nothing abnormal. The liver was palpable and was about one finger's breadth below the costal margin. The nervous system was not disturbed. Urinalysis was negative.

*Treatment.*—The treatment consisted of counterirritation, baths, expectorants and the use of polyvalent vaccines. After the fifth day of treatment, the temperature dropped. Many of the inflammatory symptoms disappeared. Daily observation had shown the variability of the pulmonary phenomena, depending on the appearance of new foci of infection and their disappearance often on the same day. The foci persisted in the bases, especially on the right base; rather severe bronchitis also persisted.

At the end of the third week the patient was discharged cured. There was a small gain in weight.

*Readmission.*—Four weeks later, the child was readmitted with fever and cough. On the day of admission the temperature was 102 F. The following day the temperature had dropped to normal and continued so. Examination of the lungs showed only a few diffuse râles. Two weeks later, the child was discharged again as cured.

*Comment.*—The striking feature of the case was the fleeting character of a definitely established bronchitis and broncho-alveolitis, and the ease with which it disappeared and reappeared in various parts of the lungs.

CASE 2.—*History.*—J. M., a boy, aged 7 years, an Argentinian, was admitted to the hospital on July 19, 1924. His parents were living and well; one child was living, and two children were dead. There was no history of tuberculosis in the family. The patient had always been considered well; he had had measles at the age of 6 years. His present illness was of seventeen days' duration, and began with vomiting, fever, fatigue and cough. Vomiting ceased the second day, but the fever and cough continued.

*Physical Examination.*—The child was in a poor state of nutrition; muscular development and panniculus adiposus were fair. The skin was dry and shrunken. Over the anterior and dorsal regions of the chest there was a pigmented area due to local medication. There was some enlargement of the cervical glands but no general adenopathy. The head was normal. The pupils reacted well to light and in accommodation. The mucous membranes were pale; the fauces were clear. There was considerable suprasternal retraction. The thorax was symmetrical and elastic. Respiration was costo-abdominal. There were tachypnea and an annoying cough without much expectoration. The voice was hoarse. Respiratory excursions were diminished. Vocal fremitus was present over the right lung posteriorly, but not over the left. There was no dulness over the area of the left lung, but slight dulness over the apex and hilum region of the right lung was noted. Auscultation showed coarse breath sounds over the left lung and definite tubular breathing over the right lung. Over the shoulder blade there was a focus of fine, subcrepitant râles. Subcrepitant râles and tubular breathing were heard over the entire involved area of the right lung. Percussion showed no dulness. Bronchial breathing was heard over the anterior part of the left lung, but there were no râles. The circulatory apparatus showed nothing abnormal. The pulse was regular and of good volume. The abdomen and abdominal organs showed nothing abnormal. The knee reflexes were exaggerated. Two Pirquet and several Mantoux reactions were negative. There was no expectoration. Examination of

the blood showed slight secondary anemia. The Wassermann reaction was negative. Urinalysis showed nothing abnormal.

A week after admission, diminished resonance was found over the entire right side of the thorax posteriorly. At the apex of the scapula tubular breathing was heard with pectoriloquy and egophony. Lower down, abundant crepitant râles were heard; also friction rubs over the entire area, which previously was clear.

*Treatment.*—Guaiacol carbonate and counterirritation to the chest were given. The temperature dropped to normal; the general condition improved, and the cough diminished. The râles and friction sounds heard over the right side of the chest increased from day to day, particularly over the base. Polyvalent vaccine was given every day. Five tuberculin tests made at different times were negative. The tubular breathing gradually disappeared, and the friction rubs and râles gradually lessened in quantity. Apyrexia continued. There was slight dulness on percussion over the right base. After the fourth week no abnormal breath sounds were heard in the entire thorax. Examination a month later still showed slight dulness of the right base without abnormal breath sounds. There was no cough. The appetite was good, and the child had gained in weight considerably.

*Comment.*—The interesting features about this case are the prolonged course, thirty-five days, the variability in the extension and intensity of the process, and the persistently negative tuberculin reactions resulting from progressively increasing dosage.

CASE 3.—*History.*—E. B., a boy, aged 11 years, was admitted to the hospital, Aug. 11, 1925. His mother was well, his father was an old alcoholic patient, an inmate of a hospital for the past year on account of liver trouble with ascites. There were three other children, all of whom were well. The mother had had no miscarriages. The patient had been well during infancy; he had had pertussis and measles at a later age, with complete recovery. There was no other illness.

The present illness began eight days prior to examination, with vomiting and slight fever. Two days before coming to the hospital he experienced a sharp pain over the base of the left side of the chest. A dry cough developed, which finally became catarrhal. Both symptoms, the pain and the cough, persisted. Moderate fever continued. Slight dyspnea was constantly present, coincident with the "stitch in the side." According to the mother, the sputum was yellowish white. Anorexia was present. The stools were normal. The urine was scanty, but normal.

*Physical Examination.*—The child showed development corresponding to his age. The skin was white, and showed numerous pigmented scars. Panniculus adiposus was moderate. There was slight general glandular enlargement. The skeletal development was fair. There was slight lateral scoliosis to the right. The head was normal. The facies showed indifference and apathy. The eye reflexes were normal; the pupils were equal and reacted to light and in accommodation. The mucous membranes of the mouth were dry. The teeth were in good condition, but showed marked malocclusion. The tongue was heavily coated. The tonsils were large. There was a moist cough, with copious greenish, frothy expectoration. The thorax was asymmetric, the right side showing enlargement. There was slight vocal fremitus over the right lung posteriorly, diminishing toward the base. Percussion showed slight dulness over the base. Respiration was increased and slightly labored. On auscultation some tubular breathing was heard near the base, and some inspiratory râles were noted. There was no bronchophony or pectoriloquy. The left lung was normal, except for a slight dulness over the base. Tubular breathing was heard over this area. On deep inspiration and during attacks of coughing, a few fine crepitant râles were heard. These could also be heard in the left axilla. The anterior part of both lungs, except for a few coarse râles over the right side, was normal. The pulse was regular and of good volume. The heart showed no enlargement and gave normal sounds. The abdomen was prominent and distended; palpation was not painful. The liver and spleen were not felt. The reflexes were normal. Under the old classification of Grancher, this patient would have been classed as having a case of splenopneumonia.

*Course of Illness.*—Slightly more than one week after admission, there was a zone of dulness beginning over the left shoulder blade and extending down to the base. There were tubular breathing, bronchophony and pectoriloquy. Râles were absent. Traube's space remained perfectly clear. Pleural puncture, undertaken two days later, gave negative results. Irregular fever, the temperature never exceeding 101 F., continued. Four injections of polyvalent antipyogenic vaccine were given, without any particular result. Sputum examination showed no tubercle bacilli, but did show numerous organisms of *Micrococcus catarrhalis* and pneumococci.

The third week after admission, the irregular fever continued. A marked retraction of the left side of the chest, with marked dorsal scoliosis and bulging of the right side of the chest, were noted. All the symptoms of the splenopneumonia of Grancher persisted. Numerous friction rubs were heard on deep inspiration. Sputum examination showed no tubercle bacilli. Examination of the blood gave a white cell count of 12,656, with 84.3 per cent polymorphoneutrophils and 14.3 per cent lymphocytes. The hemoglobin content was 50 per cent. The Wassermann reaction was negative.

The temperature dropped to normal and continued so up to the time of the patient's discharge from the hospital. He was seen again in the outpatient department about six weeks after the onset of his illness. There was an elevation of temperature to 102 F. in the afternoon. Local signs were about the same, namely, dulness, tubular breathing, râles, friction rubs, bronchophony and pectoriloquy. Hygienic and dietetic treatment was continued, and epinephrine and calcium preparations were given internally. A month later the patient was again brought for examination. His general condition was much better. There was no elevation of temperature; his color was good, and the skin and mucous membranes were clear. There was still a slight diminution of resonance over the left side of the chest from the shoulder blade to the base. The breath sounds were normal. All tubular breathing and bronchophony had disappeared. A few crepitant râles could still be heard on deep inspiration. The scoliosis had disappeared to a large extent. Three weeks later the child was seen again; all symptoms had disappeared and he was entirely well.

*Comment.*—The interesting feature about this case is the complete recovery in spite of the prolonged course, and the pronounced retraction of the left side of the chest with an extreme degree of scoliosis, both dorsal and lateral, and corresponding deformity of the right side of the chest.

Case 4.—*History.*—E. G., a boy, aged 12 years, an Argentinian, was admitted to the hospital, June 17, 1925. His father had had lung trouble for the past twelve years; his mother was well; she had had one abortion. Eight children were living and well. The patient was born at full term; birth was normal. He received mixed feeding. He had had measles at the age of 7 years.

The present illness began two days before coming to the hospital. The temperature became elevated; there were sharp pains in the left side and back, slight cough, some dyspnea and slight headache. There was no vomiting.

*Physical Examination.*—The patient was well nourished, the skin was clear; skeletal and muscular development were good; slight glandular enlargement in the axillary, neck and inguinal regions was present. The head was normal. There was no visible dyspnea. Slight cyanosis was visible in the ears and lips. The pupils were equal and reacted well to light. The mucous membranes were normal; the tongue was heavily coated. The tonsils were normal in appearance. The thorax was symmetrical. Respiration was costal in type, 40 to the minute. There was diminished respiratory excursion on the left side. The posterior part of the lungs showed good resonance over the apex of the left lung and over the entire right lung from the apex to the base. Over the left lung there was an area of dulness, beginning at the spine of the scapula and extending about four finger-breadths below the angle of the scapula. From that point on down there was again clear resonance. On auscultation, expiratory subcrepitant râles were heard. Slight bronchophony and pectoriloquy were present. The anterior part of both

lungs was normal. In the left upper axillary region slight dulness and impaired resonance were noted. No abnormal breath sounds were heard. The heart was normal in area and sounds. The pulse was regular and of good volume. The abdomen was rather tense. There was slight tenderness in the right iliac fossa. The spleen and liver were not palpable. All reflexes were normal. Two days after admission the dulness extended to the left base. In the area covered by the shoulder-blade and up to the vertebral column, breathing was tubular. Subcrepitant râles were heard, and there were some friction rubs. There was no vocal fremitus. There was diminished entrance of air to the base. Over the base of the right lung there was a small focus of crepitant râles and slight tubular breathing. The urinalysis was negative. Five days later there remained dulness, confined to an area extending from the lower end of the left scapula to the vertebral column. There were no abnormal sounds on auscultation. The temperature, which had gone down, became slightly elevated. A Mantoux test (0.001) was negative.

*Course of Illness.*—Two days later, tubular breathing and a few friction rubs were again heard at the left base. The roentgenogram showed a dense shadow over the entire left lung. The diaphragmatic excursion was somewhat diminished. Within the next ten days the clinical symptoms varied a great deal. The tubular breathing and the râles disappeared and reappeared day by day. There was a slight retraction of the left side of the chest near the base. Respiratory excursion was lessened. There was tubular breathing in the left interscapular space; egophony and pectoriloquy were also noted. There were râles and friction rubs over both bases. There was less resonance over the left thorax, particularly from the crest of the shoulder-blade down to the base. Traube's space was clear. The cough was more aggravated and was accompanied by purulent expectoration. The fever curve was irregular. As part of the treatment, two complete series of the polyvalent vaccine of Dr. Nal of the Hygienic Institute were given, without any effect. Three Mantoux tests given in increasing dosage were negative. The general condition of the child was satisfactory. The appetite was fair, and there was an increase in weight. Bacteriologic examination of the sputum showed pneumococci in large quantity, some *Micrococci catarrhalis* and short chain streptococci. There were no tubercle bacilli.

A second roentgenogram, taken two weeks after the first, still showed a shadow over the left side, much the same as it did the first time. There was diminished respiratory excursion of the right lung at the base and also diminished resonance. There had been no elevation of temperature for five days.

*Comment.*—The striking features of this case are again the great variability from day to day of a fairly severe inflammatory process, the absence of tuberculous infection and of pleural effusion. Noteworthy, also, is the ineffectiveness of vaccine therapy.

CASE 5.—*History.*—M. M. M., a girl, aged 10 years, an Argentinian, was admitted to the hospital, July 20, 1925. Nothing is known of the family history. The child had been in an orphanage for the past two years. She had always been well during that time. The patient had been ill for two days before coming to the hospital with fever and slight cough; she also complained of pain in the left side of the chest.

*Physical Examination.*—The child was well developed and in a state of good nutrition. The skin was clear. There was slight glandular enlargement. The head was normal. The mucous membranes were a good color. The tongue was heavily coated; the throat was red. The chest was well formed. There were slight dyspnea and a frequent spasmodic hacking cough. Over the right lung posteriorly there was an area of dulness extending from the shoulder-blade down to within 5 cm. of the base. The posterior part of the left lung showed diminished resonance, but no actual dulness. Over the area of dulness in the right lung a focus of the fine moist râles was heard. There was no tubular breathing. Over the left lung a few fine crepitant râles were heard, and over the base a few friction rubs. The right axillary region was clear. The left region was dull,

and fine crepitant râles were heard. The anterior portion of both lungs was clear. The heart was normal in area and in sounds. The pulse was regular and of good volume. The abdomen was normal. The liver and spleen were not palpable. The sensorium was clear; the pupils were equal and reacted to light and in accommodation. The reflexes were all present and seemed normal.

*Course of Illness.*—The day following admission, the right lung showed tubular breathing, bronchophony and pectoriloquy, in addition to numerous moist râles. The focus in the left axilla remained about the same. Three days later the tubular breathing over the right lung had disappeared and only rough breathing remained. Pleural friction rubs could be heard in the middle portion of the right lung. Subcrepitant râles were heard in both lungs at deep inspiration. Blood examination showed nothing abnormal. Within the next two weeks the pulmonary symptoms showed frequent change. The bronchial breathing was present at times; at times it was absent. The temperature remained normal for a few days and then again rose to 102 F. There was not much change in the lung symptoms. This condition continued for about two weeks, after which period complete recovery set in. The characteristic feature of the condition was the fleeting and transitory type of the lung phenomena.

CASE 6.—*History.*—E. C., aged 7 years, an Argentinian, was admitted to the hospital, Nov. 27, 1924. The parents and six other children were well. No children had died, and there had been no miscarriages. The patient's birth had been normal, at term. He had had measles at 3½ years and diphtheria a year and a half before coming to the hospital.

The present illness began eight days prior to examination, with high fever and dry and persistent cough. For three days there was pain in the lower part of the left side of the chest and in the umbilical region.

*Examination.*—There was loss of appetite and slight diarrhea. The child was undernourished and showed some evidence of rickets, such as rosary and pigeon breast. The epiphyses were enlarged, and there was deformity of the tibial bones. The skin was pale, and there was slight general glandular enlargement. The head was large, but otherwise not abnormal. The mouth, nose and throat were normal. The thorax showed good expansion. Vocal fremitus was normal. There was diminished resonance over the left thorax and dulness from the left shoulder-blade downward. The right side of the chest was clear. Inspiratory and expiratory tubular breathing over the area of dulness, and numerous râles and friction rubs were noted. Diminished breath sounds were heard over the entire affected area. The axillary regions and the anterior parts of the lung showed nothing abnormal. There was no dyspnea, but a dry cough. The cardiac area and the heart tones were normal. The pulse was regular and of good volume. The abdomen was normal. The liver was slightly enlarged. The spleen was not palpable.

*Course of Illness.*—Six days after admission, the temperature dropped to normal. The lung symptoms had practically disappeared. Only a slightly diminished resonance of the left base remained. The striking feature of this case, again, was the fleeting character of all lesions.

CASE 7.—*History.*—A. M. A., a girl, aged 7 years, an Argentinian, was admitted to the hospital, June 6, 1925. Her father died of asthma; her mother was well. There were four children living, all of whom were well. There had been no deaths or no abortions. The patient was born at term, and was breast-fed. She had had measles at the age of 7 years, followed by pertussis. She had had a fracture of the left femur at the age of 4 years. The child had been ill for two days before admission to the hospital, with an elevation of temperature to 103 F. and a severe cough.

*Physical Examination.*—The patient was well developed. The head was well formed. There was some labored breathing. The lips were dry; the tongue was coated. There was a dry, almost continuous, cough, accompanied by pain and dyspnea. The left lung showed normal resonance. Over the right lung there was

dulness from the shoulder-blade to the base. This also extended into the right axilla. Auscultation over the left lung showed nothing abnormal. The right lung showed pronounced tubular breathing over the shoulder-blade, and when the child coughed, numerous subcrepitant râles were heard over the spine of the scapula. Some tubular breathing and a few râles were also heard over the anterior part of the lung. The heart was normal in area and in sounds. The abdomen was somewhat tender to the touch. The liver and spleen were not felt. The child was dyspneic and had a drawn facies. There was marked prostration, and a tendency to drowsiness. The reflexes were normal. The child complained of pain if moved. The pupils reacted well to light and in accommodation. There was a slight leukocytosis and diminished hemoglobin; otherwise the blood picture was fairly normal.

*Course of Illness.*—The temperature continued high. The cough was more severe. The pronounced tubular breathing continued. The râles were increased and crepitant. A large inflammatory focus was present in the lower lobe of the lung. Ten days after admission, the physical phenomena of the focus in the right lung were well marked. A focus of fine râles, but without tubular breathing, was also heard in the upper part of the left lung near the shoulder-blade. Eight days later, disseminated râles were still heard. Tubular breathing was much diminished. It could be heard only in the right lung. The rest of the lung showed coarse breathing. There were a few coarse râles in the base of the left lung.

Three weeks later the child was discharged completely cured.

CASE 8.—*History.*—V. A., a boy, aged 4½ years, an Argentinian, was admitted to the hospital, Oct. 21, 1924. His parents said they were well. There were three other children, one of whom was treated for hereditary syphilis and bronchiectasis. One child died at the age of 6 months. The mother had had two abortions. The patient was breast fed for one year; he was frequently brought to the outpatient department for the treatment of fever and cough. He had had measles two weeks prior to examination. Fever and cough had continued since the attack of measles. The temperature varied between 102 and 103 F.

*Physical Examination.*—The child was feeble and undernourished. The skin was dry. The chest showed a distinct rosary and Harrison's groove. There had been some nosebleed. The lips were dry and covered with sordes. There was a frequent and severe cough; dyspnea was not noted. There was slight impairment of resonance and resilence of the left base. The right base presented a focus of subcrepitant râles. There were also some diffuse bronchial râles over the anterior part of the chest. The axillary region was normal. The heart was normal in area and in sounds. The pulse was regular and of good volume. The abdomen was normal. The liver was slightly below the costal margin. The spleen was not felt. The Mantoux test was negative.

*Treatment.*—Counterirritation, moist compresses and expectorant mixtures were given. Two days later the temperature dropped to normal. On auscultation abundant pleural friction rubs could be heard over the lower part of both sides of the chest. Two days later these were confined largely to the bases of both lungs. Fine râles could also be heard, and in the left base a small area of tubular breathing. Four days later all symptoms had disappeared, except a few fine subcrepitant râles in the left base, and these were heard only on deep inspiration.

*Comment.*—The striking feature in the case is the fleeting transitory character of the pulmonary inflammation and of all the physical signs.

CASE 9.—*History.*—A child, aged 21 months, whose parents were well, had been well up to a month prior to examination. Since then, the parents noticed almost constant fever and a persistent dry cough.

*Physical Examination.*—Examination of the chest showed pronounced dulness extending over the entire posterior part of the left thorax. Traube's space remained clear and resonant. There was tubular breathing throughout the left

side, but it was particularly pronounced over the scapula. There was complete absence of râles or friction rubs over both sides of the chest. The child was dyspneic, but was not cyanotic. All other organs were normal. Pleural puncture yielded no fluid. The Pirquet reaction was negative.

*Treatment.*—Five different injections of polyvalent vaccine were given during the course of the illness. The chest symptoms continued unchanged and gave a decided impression of a pleural effusion. There was still absence of respiratory sounds, but over the spine of the shoulder-blade tubular breathing could now be heard. A few days later, a second paracentesis of the chest was performed, again with negative result. Examination of the chest at this time showed that the dulness was considerably diminished except in the left base. Air was entering the lung freely. The tubular breathing had disappeared except for an area over the shoulder-blade.

Three weeks later the condition was unchanged, except that air now entered the lung freely down to the base. The temperature varied between 98.6 and 101 F. The child ate well. The cough was much improved. There was still some tubular breathing over the base and a focus of crepitant râles. A month later, and two months since the beginning of the process, the child was free from fever. Dulness persisted in the left base. No tubular breathing was heard, but a few pleural friction rubs on deep inspiration. A few days later they seemed more extensive and were also heard over the left shoulder-blade. A week later all signs had disappeared. The child continued free from fever. The general condition showed steady improvement. Another Pirquet test applied at this time was negative.

*Comment.*—The striking feature of the case was the prolonged course of over two months; the rather definite evidence of pleural effusion with absolutely negative results from chest puncture; the complete cure and recovery of the patient, with no evidence of latent or active tuberculosis.

# STUDIES IN SCARLET FEVER

## I. THE DICK TEST *

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The question of any diagnosis centers about either clinical judgment or some laboratory test. In the past, many cases of streptococcus infection other than scarlet fever have been labeled as scarlatina by physicians, because there was no definite method of making an absolute diagnosis. If a person had a rash associated with a sore throat, and the rash looked somewhat similar to that of scarlet fever, then for all practical purposes the patient was considered as having the disease. This was the stage when Schultz and Charlton first described their phenomenon. Briefly, the intradermal injection of a certain amount of convalescent scarlet fever serum into a patient with a rash of acute scarlet fever caused local blanching or local cure at the site of injection. If the serum of a person suspected of having scarlet fever was injected into the skin of a patient with acute scarlet fever with a rash and caused no blanching, the supposition was that there were no antibodies present in the serum injected, and the chances were that the rash of the suspected person was that of scarlet fever. Especially was this so if subsequently the serum of the latter began to show blanching qualities. Blake and Trask,[1] Dochez,[2] Birkhaug [3] and Toomey and Nourse,[4] all have investigated this phenomenon and have found essentially the same results as Schultz and Charlton.

We soon found, however, that this was not an absolutely and constantly dependable test because, first, as we will show in further papers, the convalescent serum of a patient who had recovered from scarlet fever did not always blanch the rash of a patient with acute scarlet fever; secondly, not all patients with rashes show the same amount of

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1. Blake, F. D.; Trask, J. D., and Lynch, J. F.: Treatment of Scarlet Fever with Scarlatinal Antistreptococcic Serum, J. A. M. A. **82**:712 (March 1) 1924.

2. Dochez, A. R.: Etiology of Scarlet Fever, Medicine **4**:251 (Aug.) 1925.

3. Birkhaug, K. E.: Studies in Scarlet Fever: Studies Concerning Blanching Phenomenon in Scarlet Fever, J. Clin. Investigation **1**:275 (Feb.) 1925.

4. Toomey, J. A., and Nourse, J. D.: Extinction Tests in Scarlet Fever, Am. J. Dis. Child. **27**:95 (Feb.) 1924.

reaction with the same serums in the same amounts; thirdly, certain types of papulated scarlet fever show little or no reaction when injected, and fourthly, the same skin in many instances would show different grades of reaction with the different antitoxins from the various commercial houses, even though the amount injected contained approximately the same dose of antitoxin element.

The relative amount of immunity of the patient who has the disease and the relative amount of antitoxin injected are factors so variable that there can be no unity on which any one can formulate a definite hypothesis. The reactions, however, do in a measure explain many of the phenomena associated with the disease, but because of the exceptions we believe that the Schultz-Charlton test cannot be used in an absolute sense, either as a test to determine the dosage of therapeutic serums or as a test to rule out scarlet fever.

The Dick [5] test followed, and in this paper we make an attempt to evaluate our experiences in more than 3,500 cases. The reactions of this test are comparable to those following the Schick test for diphtheria, in that the patient contracts a local attack of the disease after the injection, which is confined to a few centimeters of skin; a subject is considered susceptible who shows a positive reaction to a certain predetermined amount of material injected intradermally.

The test is extremely specific, 1 cc. of the scarlet fever toxin being sufficient material to make from 17 to 20,000 tests, each of 0.1 cc. The fresh toxin is standardized on human beings, each new batch being tried out in test solutions of various strengths on susceptible subjects. (Except when otherwise indicated, the material used in the following experiments has been received from the Dicks, the toxin being made up fresh as needed.)

By a 4 plus reaction is meant an area of erythema with induration measuring 3 cm. or over, in diameter; a 3 plus reaction, an area of erythema 3 cm. or over, without induration; a 2 plus reaction, an area of erythema from 2 to 3 cm. in diameter, without induration. The controls in this series were all negative after twenty-four hours.

## EXPERIMENTAL WORK

EXPERIMENT 1.—This experiment was performed to ascertain the Dick reaction on patients admitted to the hospital.

Fifteen hundred and seventy patients have had Dick tests made on admission. In this group one hundred and sixty-two were adults, and the remainder were children under 12 years of age. Of the adults, thirty-two (or 19.7 per cent) had positive reactions. One hundred and two children under 1 year were tested, and

5. Dick, G. F., and Dick, G. H.: Skin Test for Susceptibility to Scarlet Fever, J. A. M. A. **82**:265 (Jan. 26) 1924. Zingher, Abraham: Dick Test in Normal Persons and in Acute and Convalescent Cases of Scarlet Fever; Immunity Results with Scarlet Fever Toxin, J. A. M. A. **83**:432 (Aug. 9) 1924.

sixteen (or 15.6 per cent) gave positive reactions. The remaining 1,306 patients were from 1 to 12 years of age. Seven hundred and twenty-two (or 55.2 per cent), gave positive reactions.

EXPERIMENT 2.—This experiment was performed to ascertain the response to the Dick test on the same patients after a long interval of time.

On Oct. 6, 1924, eighty-nine nurses, twenty-four physicians, and twenty-two attendants and employees, one hundred and thirty-five in all, were tested, the reactions being listed in table 1.

In July, 1925, seven months later, the same group again received injections except three attendants who had left the hospital employ in the meantime, making a total of 132 injected.

In April, 1926, the same group received another injection. This time the group had been depleted by ten persons, making the total number 122 retested after one and a half years had elapsed.

The reactions were as follows: Twenty-nine, or 100 per cent, again gave 4 plus reactions; four, or 100 per cent again gave 3 plus reactions; three, or 75 per cent, 2 plus; eight, or 100 per cent, 1 plus, but one of these had a 2 plus reaction nine months previously, and one of the 1 plus reactions became negative in this series, the remaining being negative. This experiment was repeated each time with practically identical results. The Dick tests, performed eighteen months afterward, were essentially the same as the original tests.

EXPERIMENT 3.—The object of this experiment was to ascertain when antibodies first appeared in patients with scarlet fever as evidenced by the Dick test.

TABLE 1.—*Comparison of Reactions with Dick Tests (After Long Time Intervals)*

| Date | Number Tested | Reactions | | | | | | Original Reactions on Remainder | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ± | 1+ | 2+ | 3+ | 4+ | Neg. | ± | 1+ | 2+ | 3+ | 4+ | Neg. |
| 10/6/24 | 135 | — | 10 | 5 | 5 | 31 | 84 | .. | .. | .. | .. | .. | .. |
| 7/7/25 | 132 | — | 7 | 5 | 5 | 31 | 84 | — | 10 | 5 | 5 | 31 | 81 |
| 4/1/26 | 122 | — | 8 | 3 | 4 | 29 | 78 | — | 8 | 4 | 4 | 29 | 77 |

Four hundred patients with scarlet fever were studied; three hundred and fifty-one, or 87.7 per cent, developed negative Dick tests from eight to fifteen days after the rash appeared, twenty-two, fifteen to thirty days after; ten had negative Dick tests in less than sixty days, and seven patients with frank scarlet fever did not have a negative Dick test after six months. (Two of the latter subjects, 1 physician and 1 nurse, again developed scarlet fever within the year.)

EXPERIMENT 4.—The reactions of the same person to the toxin and to the original unheated broth in which no organisms had been grown were compared in this experiment.

Of one hundred and thirty persons who had 4 plus reactions, each person received injections twice, in one place with 0.1 cc. of the toxin and in another place with 0.1 cc. of the original broth (received from the Dicks). The reactions with the toxin were the same as before, all 4 plus. There were two subjects who had a 2 plus pseudoreaction about the site of the broth injection after twenty-four hours; the area was not inflamed or raised, but appeared more like wheals.

EXPERIMENT 5.—An attempt was made to determine whether or not there was any difference in the skin reaction to the original broth and to boiled toxin.

The group that comprised experiment 4 was again used. They received injections three times intradermally in the forearm. The injections were 0.1 cc. scarlet fever toxin, 0.1 cc. of boiled toxin and 0.1 cc. of the original broth. The reactions were again identical with the toxin, and the same two persons showed a reaction to about the same degree in the area about the site of the original injection of broth and boiled toxin.

EXPERIMENT 6.—This was a repetition of experiment 5, using an additional injection as outlined.

The one hundred and fifty-one subjects receiving injections, however, were different from those of experiments 6 and 7. The injections were as follows: first, 0.1 cc. of toxin received from the Dicks; second, 0.1 cc. of the original broth (Dick's); third, 0.1 cc. of the boiled toxin; fourth, 0.1 cc. of toxin from Pryer's organism. The reactions of these cases are tabulated.

EXPERIMENT 7.—This experiment was performed to compare the skin reaction in the same subject with various test materials of other manufacturers.

Fifty-two persons with a known reaction of 4 plus received injections with 0.1 cc. of test toxin received from the Dicks and 0.1 cc. each of test toxin of three other manufacturers, making five injections in each subject (one being a control). Care was taken to exclude the violent reactors from this group. The reactions were not the same; one test material produced from two to three times the reaction of the ordinary Dick test. The original Dick toxin gave 100 per cent positive reactions, while toxic material of the other two manufacturers gave 67 and 51 per cent positive reactions. (We must state, however, that the last test material with the 51 per cent reactions was kept at room temperature for one to two days before being used.)

TABLE 2.—*Reactions of One Hundred and Fifty-One Subjects to Injections of Various Toxins* *

| | ± | 1+ | 2+ | 3+ | 4+ | — |
|---|---|---|---|---|---|---|
| **Eighteen Hours Later** | | | | | | |
| Injection 1. 0.1 cc. Dick's toxin reactions | 13 | 17 | 18 | 33 | 28 | 60 |
| Injection 2. 0.1 cc. original broth (Dick) reactions | 10 | 12 | 10 | 12 | 4 | 103 |
| Injection 3. 0.1 cc. boiled toxin reactions | 9 | 4 | 8 | 9 | 4 | 117 |
| Injection 4. 0.1 cc. Pryer's toxin reactions (Am. J. Pub. Health **15**: 847, 1925) | 3 | 22 | — | — | — | 126 |
| **Thirty Hours Later** | | | | | | |
| Injection 1. 0.1 cc. Dick's toxin reactions | 13 | 17 | 18 | 33 | 28 | 60 |
| Injection 2. 0.1 cc. original broth (Dick) reactions | 4 | 3 | 0 | 0 | 0 | 144 |
| Injection 3. 0.1 cc. boiled toxin reactions | 2 | 2 | 0 | 0 | 0 | 147 |
| Injection 4. 0.1 cc. Pryer's toxin reactions | 2 | 0 | 0 | 0 | 0 | 149 |

* Each individual received injections four times, total 151.

EXPERIMENT 8.—This test was undertaken to demonstrate the difference in the skin reaction between the country and the city person.

One hundred persons born and living in the city were tested with a Dick test and their reactions were compared with those of one hundred persons born and living in the country. In the first instance, the percentage of positive Dick reactions was 14 per cent, while in the persons born and living in the country the positive reaction was 54 per cent.

EXPERIMENT 9.—This experiment was performed to determine whether the general or local reaction was as great with intramuscular as with intracutaneous injections.

One hundred and forty persons whose reactions to the Dick tests were negative, and who had received injections with test doses of the Dick toxin in the usual percentages (from 0.1 cc. 1-1750) intramuscularly with negative results, were used for this experiment. The injection value was increased to 250 skin test units, and in only two patients was there any reaction; in these two there was some local induration and elevation of temperature to 101 F. for one day. This experiment was made to determine whether some minimum dose of toxin could be established which would cause some local or general reaction, which could be taken as evidence of susceptibility, the injection thus serving two purposes, namely, as a test of susceptibility, and as the first immunizing dose. This would be analogous to the method of immunizing against diphtheria, as

introduced by Gerstenberger,[6] who ignores the primary Schick test in certain age groups, and gives immunizing doses at once, using the Schick test later to ascertain the presence or absence of acquired immunity.

EXPERIMENT 10.—This experiment was performed to ascertain what effect room temperature would have on the toxin.

Toxic material was made up and tried on a group of twenty persons with known 4 plus reactions; all were again 4 plus. A portion of the material was then placed on ice for three months, and a portion was placed at room temperature for three months; the group was then retested. Each person received 0.1 cc. of each toxin which had been thus prepared, in addition to the control of boiled toxin. The reactions to the material which had been kept on ice were all 4 plus. The toxin kept at room temperature gave positive but decreased reactions from a plus minus to a 2 plus, none approaching the 4 plus quality of the original experiment.

EXPERIMENT 11.—The object of this experiment was to ascertain the reaction when the same needle was used for the test and then for the control.

One hundred and thirty subjects with 4 plus reactions, the same group as in experiment 4, were tested. The injection of the toxic material was given, and the same needle was used to inject the control mixture. One hundred and twelve of the one hundred and thirty persons, or 86.1 per cent, showed reactions varying from a faint positive to a definitely 4 plus reaction about the site of injection of the control mixture, showing that in the extremely susceptible person, a fraction of a drop of unkilled toxin may cause a definite reaction and a false positive control.

EXPERIMENT 12.—This experiment was performed to test out the reactions obtained from toxin heated at varying intervals.

Eighty-two subjects were selected who had 4 plus Dick tests, and negative broth controls. The control mixtures used in this experiment were batches of toxin simply inactivated at 56 C. for fifteen minutes (lot 1), for thirty minutes (lot 2) and for one hour (lot 3). The injection of unboiled toxin was again followed by 100 per cent reactions. Eleven had 2 to 4 plus reactions about the toxin inactivated for fifteen minutes. Seven subjects had 1 to 4 plus reactions about the toxin inactivated for thirty minutes, and five had 1 to 3 plus reactions about the toxin inactivated for one hour.

## COMMENT

Occasionally the boiled toxin used as a control causes a much larger reaction locally than the toxin itself. This we have found to occur in four instances of more than 3,500 persons receiving injections. In the first patient in whom this fact was noted, the boiled control caused a reaction twice the extent of the toxin injection. We thought that we had reversed the injection and were dealing with a good positive and a pseudoreaction. Repeated injections, however, confirmed the observation that in this instance, as in three others, the boiled toxin caused a greater reaction than the toxin itself, although in these four subjects the plain broth, when injected, caused only a slight reaction. These patients had received toxin antitoxin, but so had hundreds of others who had been tested. In none could we obtain any history of sensitivity; there was no familial or personal history of hives, hay-fever, eczema, angioneurotic edema or any atopic manifestation. Furth[7] found that

6. Gerstenberger: Prevention of Diphtheria, Pub. Health Nurse **13**:179, 1921.
7. Furth, J.: Antigenic Character of Heated Protein, J. Immunol. **10**:777 (Sept.) 1925.

the simple boiling of a protein sometimes changes its character so that in the untested state it may cause no reaction, while the same material heated may cause a definite reaction. We have noted some delayed positive reactions, in one instance, as long as four days. The majority, however, react within twenty-four to thirty-six hours, and are absorbed so rapidly that they must be inspected within twenty-four hours as usually recommended, but when negative they should be checked later.

Pseudoreactions to the control mixtures were common, according to some authors, but our experience is that if the toxin is actually boiled for twenty minutes, the number of pseudoreactions is practically negligible after from eighteen to twenty hours. In our series at least, the control mixtures have given us no trouble.

Fifteen nurses who contracted scarlet fever, and who had previous 4 plus reactions, showed a curious phenomenon around the site of the previous Dick test. In all instances, before the rash had appeared, the area in and around the old Dick test became reddened and stayed red until the rash appeared. Later, it became pigmented. In two instances, this reaction occurred one year after the original test. We have observed no blanching about previous Dick tests when scarlet fever has been contracted subsequently.

In five persons, the injection of the small amount of toxin necessary to cause the ordinary Dick test reaction was followed by a violent local and general reaction. Three of these subjects repeatedly received injections with small amounts of toxin. The last injection caused as great a reaction as the first. These persons (two nurses and one physician) seemed to be particularly hypersusceptible to the toxin. Curiously enough, although they gave marked positive reactions repeatedly, two of them did not develop scarlet fever while in service, although the physician had two or three attacks of streptococcic sore throat. One of these subjects had a typical scarlet fever rash break out after exposure to scarlet fever, but there was no general reaction, fever, sore throat, or any clinical sign associated with this rash.

The immunity that persons have against scarlatina at present seems to be fairly permanent, although in eight instances persons who had negative Dick tests later developed a positive Dick test within one year, two of them contracting scarlet fever, one of a very toxic type, the other a prolonged case of scarlet fever with complications. Two subjects, one a physician and the other a nurse, who had negative Dick tests about January, 1926, contracted typical scarlet fever in May and June, respectively. The Dick test was made again at the height of the rash in both instances, and it was again negative. It was repeated several times, always with negative results, although the material gave good reactions on definite positive controls.

It has been thought sometimes that we could presage the severity of a subsequent scarlet fever by the reaction found in the previous Dick test. The first nurses who gave positive reactions after receiving injections, who were not desensitized and who later contracted scarlet fever, paralleled the Dick reaction in the severity of the symptoms; i. e., the more marked the Dick reaction had been, the more marked was the scarlet fever. This parallel, however, was not constant, for in subsequent experiences the mild positive Dick reaction in many instances had a marked disease reaction; while in a few instances, the subject with a 4 plus Dick reaction had a mild attack of scarlet fever. The number of exceptions has been enough so that the only conclusion we could draw was that the majority of persons with marked positive Dick reactions probably would contract severe scarlet fever if they were exposed and contracted the disease.

In thirty-one cases of typical scarlatinal form of eruption with all the clinical signs of scarlet fever, the Dick test has been negative repeatedly. In all of these cases the first Dick test was made within eight hours after the rash had appeared. Fifteen of these persons had their prodromal symptoms within twenty-four hours after the injection, and could reasonably be supposed to have no recently formed immunity. The remainder of the patients had longer prodromal periods, sometimes extending from two to five days, so that there could have been a possibility that some immunity might have been established before the test was made.

The greatest difficulties with the Dick test lie in the method of its standardization, a method which depends on the human immune element which is so variable. Even with this difficulty, however, the Dick test will have to be used until some method, animal or otherwise, has been evolved which will make standardization more definite.

## SUMMARY

The Dick test is the best method of ascertaining individual immunity or susceptibility to scarlet fever.

Control pseudoreactions do not ordinarily occur if the control toxin is boiled for twenty minutes.

The reactions that occur about the control mixtures in a small number of cases disappear before twenty-four hours.

As a rule, persons with negative Dick tests have had negative reactions for as long as eighteen months.

# RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

## IV. ELIMINATION OF WATER THROUGH THE SKIN AND RESPIRATORY PASSAGES

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In the course of studies on the energy metabolism of children, we had the opportunity to determine the water output through the skin and lungs under standard conditions in a large group of observations. In view of the meager literature on the subject, we are presenting the results of these studies.

### REVIEW OF LITERATURE

Most investigations on the water of vaporization have been made in adults. For this reason reference will be made to only the more important contributions. Soderstrom and Du Bois [1] give a comprehensive review of the literature up to the year 1917. Using a respiration calorimeter, these authors found that at temperatures between 22 and 24 C., and at relative humidities between 15 and 40 per cent, normal men lose 24 per cent of their calories in vaporization through skin and respiratory passages. Under the same basal conditions, eight boys between 12 and 13 years eliminated an average of 27 Gm. of water per hour, losing in this manner 27 per cent of the total heat produced. Adult patients with nephritis, pernicious anemia, diabetes mellitus and typhoid fever lost approximately the same percentage of calories in vaporization as the normal subjects. They conclude that the water elimination through the aforementioned channels is but slightly affected by disease.

Since this publication in 1917, few additional studies have appeared. McClure and Sauer [2] measured the insensible perspiration from limited areas of skin (chest) in thirteen infants and found, in accord with Nieman,[3] that atrophic infants lose relatively more water in vaporization

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1. Soderstrom, G. F., and Du Bois, E. F.: Clinical Calorimetry: XXV. The Water Elimination Through Skin and Respiratory Passages in Health and Disease, Arch. Int. Med. **19**:931 (May) 1917.

2. McClure, W. B., and Sauer, L. W.: Observations Regarding the Loss of Water Vapor Through the Skin in Infants, Arch. Int. Med. **21**:428 (March) 1918.

3. Nieman, A.: Der Respiratorische Gaswechsel im Sauglinsalter, Ergebn. d. inn. Med. u. Kinderh. **11**:32, 1913.

than normal infants. Marfan and Dorlencourt [4] conclude that infants with severe diarrhea complicated by dehydration give off more water through the lungs than normal children used as controls. Siebeck and Borkowski [5] used a "Benedict absorption apparatus" with a face-mask attachment, and found that normal adults eliminate from 11 to 20 Gm. of water per hour through the lungs under basal conditions. In 1924, Hecht [6] employed a somewhat similar apparatus to determine the water exhaled from the lungs, and noted the close interrelation between water loss and body temperature. Schlüter,[7] with the aid of a cabinet which collected the moisture from the skin only (similar to the apparatus used by Schwenkenbacher [8] in 1904), determined the insensible perspiration of two normal adults, and found that when the fluid intake was reduced to a minimum before an observation, the water eliminated through the skin fell from 22.7 to 18.7 and from 18.3 to 15.3 Gm. per hour, respectively.

A number of investigators have resorted to changes in body weight to estimate the gaseous emanations through the skin and lungs. With this method, approximately from 10 to 15 per cent of the total weight loss is ascribable to the weight of the carbon eliminated through the lungs as carbon dioxide. Nobel and Rosenblüth [9] found a diminution of the insensible perspiration in myxedematous children. Freise [10] noted that changes in the water intake had a more marked effect on the water elimination through the skin of obese than of normal children. Buttenweiser [11] attributed the greater gain in weight of so-called hydrolabile children with insulin therapy to a better water retention in the tissues. Block [12] also studied the water metabolism of hydrolabile children. Roth [13] states that approximately one third of the total water lost from

4. Marfan, A. B., and Dorlencourt, H.: Exhalation of Water by Lung in Healthy Infants and in Infants with Cholera Infantum or Diarrhea, Nourrisson **10**:173 (May) 1922.

5. Siebeck, R., and Borkowski, J.: Elimination of Water Through Lungs; Relation to Water Metabolism in General, Deutsche Arch. f. Klin. Med. **131**:55 (Dec.) 1919.

6. Hecht, A. F.: Zur Kenntniss der Extrarenalen, insbesondere Pulmonalen Wasserausscheidung, Ztschr. f. Kinderh. **38**:193, 1924.

7. Schlüter, E.: Heat Regulation and Loss of Water by Skin During Restriction of Fluid Intake, Arch. f. d. ges. Physiol. **210**:432, 1925.

8. Schwenkenbacher, A.: Ueber die Ausscheidung des Wassers durch die Haut von Gesunden und Kranken, Deutsches Arch. f. klin. Med. **79**:29, 1904.

9. Nobel, E., and Rosenblüth, A.: Myxodemstudien: V. Mitteilung. Ueber den Wasserhaushaltbeim Kindlichen Myxoden, Ztschr. f. Kinderh. **39**:702, 1925.

10. Freise, R.: Ein Beitrag zur Physiologie des Wasserhaushaltes beim fettsuchtiger Kinde, Jahrb. f. Kinderh. **108**:181 (April) 1925.

11. Buttenweiser, S.: Einfluss des Insulins auf den Wasserstoffwechsel und Korpergewicht bei Sauglingen, Med. Klin. **21**:663 (May) 1925.

12. Block, W.: Wasserhaushaltsversuche bei Hydrolabilen Kindern, Ztschr. f. Kinderh. **38**:22, 1924.

13. Roth, N.: Beitrage zum Extrarenalen Wasserstoffwechsel bei Normalen und Nephritiden, Ztschr. f. klin. Med. **98**:305 (March) 1924.

the body is through the skin and lungs. Nieman,[3] in an extensive investigation in 1913, pointed out the many objections to the use of the before-mentioned method. However, in a paper which appeared within the past few months, Benedict and Root[14] measured accurately the insensible perspiration of normal, diabetic and hyperthyroid subjects with the aid of a delicate balance capable of weighing up to 200 Kg. with an accuracy of 0.1 Gm. They also made practically simultaneous measurements of the total heat production in a number of their subjects. The relationship between the two measurements was so striking that the authors constructed a straight line curve as a method for predicting the probable metabolism from the measured insensible perspiration.

A review of the literature reveals few previous attempts to measure directly the water elimination through the skin and respiratory passages of children by means of the respiration chamber. The difficult technic and numerous sources of error may account for the paucity of data.

## METHOD

A detailed description of the apparatus and technic appeared in papers I and II of this series.[15] The apparatus includes a "Benedict Cot Chamber" and "Benedict Universal Respiration Table," modified in such a manner as to determine the water elimination at the same time as the heat production of the subject. Accurate measurement of the former is difficult. Soderstrom and Du Bois[1] review fully the many sources of error, a partial list of which will appear later in the paper. Scrupulous care was taken in this study to avoid these errors as completely as possible.

Patients were studied under the standard conditions adopted by the before-mentioned authors in their work with adults. In brief, they are as follows:

The respiration chamber with its contents remains open on the night before the observation. The following morning the temperature and relative humidity of the air in the calorimeter room are noted. They ranged between 22 and 25 C. and between 36 and 60 per cent, respectively, throughout these experiments. The patient is dressed in a light-weight woolen suit of underwear, the rectal temperature is taken, he is placed in the respiration chamber and wrapped in a thin sheet. The cover of the chamber is then lowered. During a preliminary period,

14. Benedict, F. G., and Root, H. F.: Insensible Perspiration: Its Relation to Human Physiology and Pathology, Arch. Int. Med. **38**:1 (July) 1926.

15. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and Childhood: I. Basal Metabolism in Children, Am. J. Dis. Child. **31**:323 (March) 1926. Wilson, J. R.; Levine, S. Z., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: II. Ketosis and the Respiratory Exchange in Children, Am. J. Dis. Child. **31**:335 (March) 1926.

which lasts from one-half to one hour, the rate of ventilation is adjusted to maintain the relative humidity of the air in the chamber at the original level, and the device for controlling the temperature is regulated to maintain a uniform temperature. The actual experiment commences at this point. The rate of ventilation was adequate in all experiments to remove quantitatively the moisture eliminated by the subject.

This paper includes only those observations which complied with the following requirements: The relative humidity of the air in the respiration chamber changed less than 10 per cent during the observation (usually less than 5 per cent). The temperature of the air in the chamber changed less than 1 C. The rectal temperature of the patient varied less than 1 F.

In accordance with the method of Atwater and Benedict,[16] the results are expressed in terms of percentage of heat lost in vaporization. At temperatures between 22 and 25 C., the vaporization of 1 Gm. of water requires 0.584 calories. The amount of water eliminated by the patient during an experimental period is calculated from the gain in weight of the sulphuric acid absorbers, correction being made for changes in the vapor content of the chamber. The latter is determined by analyzing 10 liter residual samples of air withdrawn from the chamber at the end of each period.

### ALCOHOL CHECKS

The alcohol checks for the year 1924 to 1925 appear in the first paper of this series. In that year, the apparatus measured the water produced by the burning of alcohol, with an average error of + 2.9 per cent. The results of the checks for the following year appear in table 1. The average error in the water determination fell to + 0.4 per cent, with a maximum error of + 2.8 per cent on Dec. 24, 1925. More rigid attention to technic may account for this reduction. These results compare favorably with those reported by other investigators.

Alcohol checks were made with the bed and clothing in the chamber, and under the same conditions as observations with patients. Notwithstanding the many difficulties encountered in the accurate measurement of the water of vaporization, we feel assured that the careful technic and the close agreement in the alcohol checks justify the acceptance of our results with a maximum error of 10 per cent, and with an average error of 5 per cent.

### RESULTS

The data include sixty-one observations of two to four hours on ten children. The histories and calorimeter data of most of the sub-

16. Atwater, W. O., and Benedict, F. G.: Experiments on the Metabolism of Matter and Energy in the Human Body, U. S. Department of Agriculture, Office Exper. Station Bull. 69, 1899.

jects have already been presented in previous reports. The data of the few remaining patients will appear shortly.

*The Water of Vaporization in Normal Children.*—Four entirely normal children were studied in twenty-eight experiments (cases 2, 3, 4 and 11). In addition, four observations each were made on one very obese but otherwise normal girl (case 7), and on one girl who had a moderate adenomatous enlargement of the thyroid gland but who was entirely free from symptoms (case 10). All determinations were made either in the postabsorptive state, or from four to six hours after a light meal under resting conditions (footnote, table 2). The children

TABLE 1.—*Alcohol Checks for Experimental Year (1925-1926)*

| | | | Water | | | Carbon Dioxide | | | Oxygen | | | Respiratory Quotient (0.667) | | Heat |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Date | Minutes | Alcohol, Gm. | Theory, Gm. | Found, Gm. | Error, per Cent | Theory, Gm. | Found, Gm. | Error, per Cent | Theory, Gm. | Found, Gm. | Error, per Cent | Found | Error | Theory Calories |
| Oct. 22 | 60 | 5.52 | 7.26 | 7.14 | | 10.55 | 10.29 | | 11.51 | 11.00 | | 0.680 | | 39.09 |
| | 60 | 5.66 | 7.44 | 7.72 | | 10.83 | 10.99 | | 11.81 | 12.15 | | 0.658 | | 40.09 |
| Average | | 5.59 | 7.35 | 7.43 | +1.1 | 10.69 | 10.64 | −0.5 | 11.66 | 11.58 | −0.7 | 0.669 | +0.002 | 39.59 |
| Oct. 24 | 62 | 7.53 | 9.90 | 9.91 | | 14.39 | 13.89 | | 15.69 | 15.05 | | 0.671 | | 53.30 |
| | 58 | 7.24 | 9.52 | 9.34 | | 13.84 | 13.69 | | 15.10 | 14.93 | | 0.667 | | 51.27 |
| Average | | 7.39 | 9.71 | 9.63 | −0.8 | 14.11 | 13.79 | −2.3 | 15.40 | 14.99 | −2.7 | 0.669 | +0.002 | 52.29 |
| Nov. 6 | 60 | 4.62 | 6.08 | 6.30 | | 8.84 | 9.40 | | 9.64 | 10.30 | | 0.664 | | 32.74 |
| | 60 | 4.70 | 6.17 | 5.83 | | 8.97 | 8.73 | | 9.79 | 9.27 | | 0.685 | | 33.25 |
| Average | | 4.66 | 6.13 | 6.07 | −1.0 | 8.91 | 9.07 | +1.8 | 9.72 | 9.79 | +0.7 | 0.674 | +0.007 | 33.00 |
| Dec. 14 | 56 | 6.09 | 8.01 | 8.26 | | 11.65 | 11.55 | | 12.71 | 12.50 | | 0.672 | | 43.15 |
| | 45 | 4.95 | 6.50 | 6.65 | | 9.45 | 9.43 | | 10.31 | 10.24 | | 0.670 | | 35.03 |
| Average | | 5.52 | 7.26 | 7.46 | +2.8 | 10.55 | 10.49 | −0.6 | 11.51 | 11.37 | −1.2 | 0.671 | +0.004 | 39.09 |
| Mar. 24 | 60 | 4.47 | 5.89 | 5.77 | | 8.54 | 8.41 | | 9.31 | 9.15 | | 0.668 | | 31.63 |
| | 65 | 4.79 | 6.31 | 6.68 | | 9.15 | 9.26 | | 9.98 | 10.65 | | 0.632 | | 33.91 |
| | 60 | 4.40 | 5.79 | 5.59 | | 8.40 | 8.24 | | 9.16 | 8.94 | | 0.670 | | 31.12 |
| Average | | 4.55 | 6.00 | 6.01 | +0.2 | 8.70 | 8.64 | −0.7 | 9.49 | 9.58 | +1.0 | 0.656 | −0.011 | 32.22 |
| Total average..... | | | 36.45 | 36.60 | +0.4 | 52.96 | 52.63 | −0.6 | 57.78 | 57.33 | −0.8 | 0.668 | +0.001 | 39.24 |

received from 350 to 400 cc. of water with the last meal. The results are summarized in table 2.

The first four children eliminated an average of 16 Gm. of water per hour through skin and respiratory passages, losing in this manner 24 per cent of their total caloric output in vaporization. The obese girl and the girl with the thyroid adenoma gave off 23 and 19 Gm. of water per hour, respectively, and the percentage of heat which they lost in vaporization exactly equalled that in the normal controls (24 per cent). The average figures for individual subjects ranged between 21 and 29 per cent. These values are identical with those obtained in adults under similar conditions by Soderstrom and Du Bois.[1]

*The Water of Vaporization in Children Suffering from Various Conditions.*—Figures for the water of vaporization under the aforementioned standard conditions are available in isolated cases of cyclic

vomiting (case 5), epilepsy (case 1), lymphatic leukemia (case 2) and diabetes mellitus (case 6). The data comprise 25 calorimeter observations of two to four hours' duration. The results appear in table 3.

These patients lost an average of 26, 20, 20 and 19 per cent of the total heat output, respectively, in vaporization of water through skin

TABLE 2.—*Normal Children*

| Case | Date | Calories per Hour | Water, Gm. per Hour | Calories Lost in Vaporization, per Cent | Remarks |
|---|---|---|---|---|---|
| 2* | 1/ 2/25 | 42.7 | 16 | 22 | Normal girl, 10⅓ years old |
| | 1/ 7/25 | 43.8 | 21 | 28 | |
| | 1/13/25 | 47.0 | 16 | 22 | |
| | 1/14/25 | 39.9 | 18 | 26 | |
| | 1/14/25 | 35.4 | 15 | 25 | |
| | 1/15/25 | 39.9 | 17 | 24 | |
| | 1/16/25 | 38.7 | 17 | 25 | |
| | 1/27/25 | 39.0 | 18 | 26 | |
| | 1/28/25 | 38.8 | 15 | 23 | |
| | 1/29/25 | 39.3 | 14 | 22 | |
| | Average | | | 24 | |
| 3* | 1/ 9/25 | 35.3 | 17 | 29 | Normal girl, 7 years old |
| | 1/21/25 | 39.0 | 19 | 29 | |
| | 1/23/25 | 35.8 | 18 | 29 | |
| | Average | | | 29 | |
| 4* | 2/18/25 | 42.8 | 20 | 27 | Normal boy, 7 years old |
| | 2/20/25 | 37.5 | 18 | 28 | |
| | 2/25/25 | 36.8 | 15 | 24 | |
| | 3/ 2/25 | 35.3 | 13 | 22 | |
| | 3/ 4/25 | 38.7 | 17 | 26 | |
| | 3/ 5/25 | 38.7 | 16 | 24 | |
| | 3/ 6/25 | 40.5 | 19 | 28 | |
| | 3/13/25 | 40.1 | 14 | 20 | |
| | Average | | | 25 | |
| 11 | 3/12/26 | 33.8 | 15 | 25 | Normal boy, colored, 6½ years old |
| | 3/15/26 | 36.7 | 13 | 21 | |
| | 3/17/26 | 32.5 | 12 | 21 | |
| | 3/18/26 | 33.5 | 13 | 22 | |
| | 3/21/26 | 35.4 | 13 | 21 | |
| | 3/22/26 | 31.5 | 12 | 21 | |
| | 3/23/26 | 34.5 | 10 | 17 | |
| | Average | | | 21 | |
| 7* | 5/ 6/25 | 54.7 | 23 | 25 | Normal girl, obese, 7 years old |
| | 5/19/25 | 54.2 | 21 | 23 | |
| | 5/20/25 | 59.2 | 23 | 22 | |
| | 5/21/25 | 58.1 | 24 | 24 | |
| | Average | | | 24 | |
| 10 | 11/16/25 | 50.0 | 22 | 26 | Normal girl, thyroid adenoma, 10½ years old |
| | 11/18/25 | 46.2 | 18 | 23 | |
| | †\|11/27/25 | 46.7 | 17 | 21 | |
| | \|11/27/25 | 65.3 | 29‡ | 26 | |
| | Average | | | 24 | |

* Histories and data of these patients appeared in papers I and II of this series.
† This observation lasted four hours, during the last two hours of which the subject exercised vigorously.
‡ This figure not included in average.

and respiratory passages. With the possible exception of the diabetic boy, they therefore gave figures which approximated the extreme average figures of the normal controls. The diabetic boy was studied on two different occasions, separated by an interval of six months. In both

series he lost a slightly lower percentage of heat in vaporization (19 and 18 per cent, respectively) than the other children. Soderstrom and Du Bois [1] give 18 per cent as the average figure of three observations for the percentage of heat lost in vaporization by a boy with mild diabetes, aged 17 years.

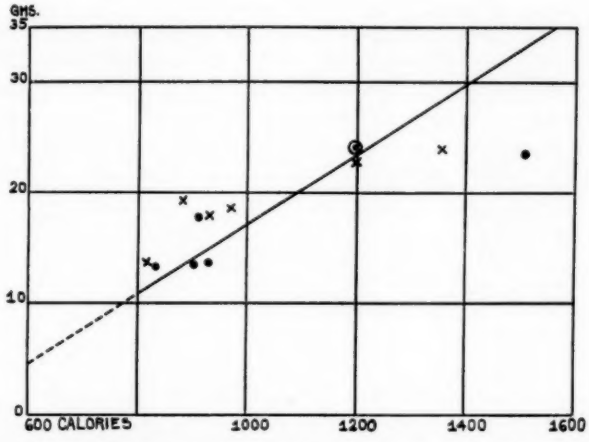
TABLE 3.—*Sick Children*

| Case | Date | Calories per Hour | Water, Gm. per Hour | Calories Lost in Vaporization, per Cent | Remarks |
|---|---|---|---|---|---|
| 1* | 12/12/24 | 36.6 | 11 | 18 | Girl, 6½ years old with epilepsy |
| | 12/15/24 | 32.4 | 11 | 19 | |
| | 12/22/24 | 33.4 | 14 | 24 | |
| | Average | | | 20 | |
| 5* | 4/15/25 | 40.6 | 18 | 26 | Girl, 7 years old with cyclic vomiting |
| | 4/21/25 | 41.6 | 16 | 22 | |
| | 4/25/25 | 41.7 | 20 | 28 | |
| | 5/13/25 | 31.7 | 15 | 27 | |
| | 5/15/25 | 35.4 | 17 | 29 | |
| | 5/16/25 | 37.2 | 15 | 24 | |
| | Average | | | 26 | |
| 9 | 12/10/24 | 63.1 | 22 | 20 | Boy, 11 years old with acute lymphatic leukemia |
| 6* | 4/10/25 | 41.7 | 16 | 22 | Boy, 10½ years old, with mild diabetes mellitus, sugar free |
| | 4/14/25 | 37.0 | 12 | 19 | |
| | 4/17/25 | 38.1 | 9 | 14 | |
| | 4/22/25 | 37.0 | 11 | 17 | |
| | 4/30/25 | 39.9 | 12 | 18 | |
| | 5/ 8/25 | 38.7 | 13 | 19 | |
| | 5/ 9/25 | 31.5 | 14 | 26 | |
| | 5/10/25 | 35.2 | 11 | 19 | |
| | 5/11/25 | 36.7 | 13 | 21 | |
| | Average | | | 19 | |
| 6 | 10/30/25 | 38.5 | 13 | 20 | Same, 11 years, basal |
| † | 11/ 4/25 | 40.5 | 12 | 14 | |
| | 11/25/25 | 37.1 | 11 | 18 | |
| | Average | | | 18 | |
| † | 10/30/25 | 52.5 | ‡15 | 17 | Exercise |
| | 11/ 4/25 | 61.4 | ‡15 | 13 | |
| | 11/25/25 | 52.4 | ‡16 | 17 | |
| | Average | | | 16 | |

* Histories and data of these patients appeared in papers 1 and 2 of this series.
† These observations lasted four hours, during the last two hours of which the subject exercised vigorously.
‡ These figures not included in average.

The second series consisted of three observations of four hours' duration. The patient rested quietly during the first two hours and exercised vigorously during the last two hours of each experiment. The exercise was sufficiently strenuous to raise the average heat production in the three observations from 38.7 to 55.4 calories per hour (43 per cent above the basal level). The heat removed from the body in vaporization rose from 7.2 to 8.9 calories per hour (10 per cent above the basal figures). As the body temperature did not change in any of these experiments, the remaining 15 calories of the extra heat produced must

have been eliminated through radiation and conduction (33 per cent). In a comparable experiment on a normal patient (case 10, on Nov. 27, 1925, table 2), exercise raised the heat production from 46.7 to 65.3 calories per hour (40 per cent above the basal level). Coincidently, the heat lost in vaporization from the skin and lungs rose from 9.8 to 16.8 calories per hour (71 per cent above the basal figures). In contrast to the observations on the diabetic boy, the rectal temperature in this experiment rose 0.8 F., indicating storage within the body of some of the extra heat.[17] Obviously, heat elimination by way of radiation and conduction was not as efficient in this patient as in the boy with diabetes.




Relation of insensible perspiration per hour to heat production per twenty-four hours. The normal children are indicated by crosses, the sick children by dots, and one normal woman by a dot enclosed in a circle. The straight line curve for predicting the probable metabolism from the insensible perspiration is copied in part from the chart of Benedict and Root.

In the chart, the values for the simultaneously measured heat production and insensible perspiration of our children are superimposed on the straight line curve suggested by Benedict and Root (footnote 14, p. 26) as a method for predicting the probable metabolism from the measured insensible perspiration. In order to make the values comparable, it was necessary to add the weight of the carbon eliminated as carbon dioxide through the lungs and skin to the water of vaporization. The weight

17. The heat stored in the body may be roughly estimated by making the questionable assumption that the rectal temperature as recorded measures the temperature of the whole body, and by using the approximate figure of 0.82 as the specific heat of body tissue.

0.44 (rise in rectal temperature in C.) × 0.82 (specific heat of body) × 31.36 (body weight Kg.) = 11.3 (calories).

In this experiment, the total heat production rose 18.6 calories per hour. Seven calories were removed from the body through increased vaporization, leaving 11.6 calories, 11.3 of which remained stored in the body.

of the carbon was obtained by deducting the average oxygen consumed from the average carbon dioxide produced per hour by the subject.

The scattered individual points are seen to approximate fairly closely the suggested curve. The results indicate that the relationship between insensible perspiration and heat production existing in adult subjects as found by Benedict and Root [14] may be extended to normal and probably to sick children. In fact, the method adopted by the afore-mentioned authors to express the relation of insensible perspiration to total metabolism and the previous method of Atwater and Benedict,[16] in which the relation is expressed in terms of percentage of total calories lost in vaporization (the method used in this paper) are essentially the same.

TABLE 4.—*Summary of Water Vaporization of Children Under Standard Conditions of Clothing, Temperature and Relative Humidity*

| Number and Age of Subjects | Number of Observations | Percentage of Calories Lost in Vaporization |
|---|---|---|
| Four normal children, 6½ to 10 years | 28 | 24 |
| One obese, but otherwise normal girl, 7 years | 4 | 24 |
| One girl with enlarged thyroid, no symptoms, 10½ years | 3 | 24 |
| Same girl, moderate exercise | 1 | 26 |
| One girl with epilepsy, 6½ years | 3 | 20 |
| One girl with "cyclic vomiting," 6½ years | 6 | 26 |
| One boy with acute lymphatic leukemia, 11 years | 1 | 20 |
| One diabetic boy, 10½ years, first series | 9 | 19 |
| Same boy, 11 years, second series | 3 | 18 |
| Same boy, second series, moderate exercise | 3 | 16 |

## SUMMARY AND CONCLUSIONS

The elimination of water through the skin and respiratory tract of ten children under resting conditions was measured in 61 calorimeter observations of from two to four hours' duration. The temperature and relative humidity in all experiments ranged between 22 and 25 C., and between 35 and 60 per cent, respectively. The technic was rigidly controlled, and we feel assured that the experimental error does not exceed 10 per cent, and is in most instances about 5 per cent.

Under the afore-mentioned standard conditions, six normal children lost an average of 24 per cent of the total heat produced in vaporization. The extreme figures for children in this group were 21 and 29 per cent. Under the same conditions, three children with epilepsy, "cyclic vomiting" and acute lymphatic leukemia, respectively, gave values close to the extreme figures for the normal controls. One diabetic boy lost a slightly lower percentage of calories in vaporization.

The results demonstrate that healthy children and most sick children (afebrile), as well as adults,[1] eliminate approximately 25 per cent of the total heat produced in vaporization through skin and lungs, and the remaining 75 per cent by way of radiation and conduction.

The close relation between insensible perspiration and metabolism previously found to exist in adults [14] may be extended to children.

# PENTOSURIA

## REPORT OF A CASE

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DETROIT

A variety of reducing substances is demonstrable under varying conditions in the human urine. In view of the danger of hypoglycemic shock as a result of nonindicated doses of insulin, it becomes a matter of more than theoretical importance to determine the nature of the substance present in the urine of a patient suspected of having diabetes. It need hardly be emphasized that a reduction of copper solutions is not sufficient for a diagnosis of diabetes. Even a blood sugar higher than normal, as in the case to be presented, may lead one astray. A frequent source of error is the presence of fructose in the urine. Occasionally, as in the present case, one is dealing with pentosuria.

While essential pentosuria is probably of more frequent occurrence than is generally recognized, the reported cases are not numerous, and the following case is that of the youngest patient on record. Pentose itself may be derived, first, from pentosans, such as gum arabic, by hydrolysis with acids; and, secondly, by hydrolysis of nucleoproteins. The source of the urinary pentose has never been satisfactorily explained, although two distinct types of pentosuria are recognized; namely, alimentary pentosuria, a temporary condition resulting from the consumption of large amounts of arabinose-containing fruits, such as cherries, plums and grapes, and essential pentosuria, which is chronic and independent of the quantity of the pentose in the diet.

Our knowledge of essential pentosuria up to the present time has been thoroughly discussed by Garrod [1] who emphasizes the fact that a large proportion of the cases described have been in Jewish patients, and that the condition has a distinct tendency to occur in several members of the same family. He also discusses the question of the congenital nature of the anomaly, its relationship to diabetes mellitus and its etiology. The following case tends to bear out certain of the major points emphasized by Garrod.

### REPORT OF CASE

*History.*—A boy, Jewish, born May 18, 1922, was brought to the office, April 14, 1925, because of pallor and loss of weight, subsequent to a griplike infection

* Received for publication, Sept. 24, 1926.

1. Garrod, A. E.: Inborn Errors of Metabolism, London, Hodder & Stoughton, 1923.

occurring about six weeks previously. The child had been under our observation as a "feeding case" and during minor illnesses since the date of his birth. He was a full term, instrumentally delivered baby, who weighed 6 pounds, 15 ounces (3,152 Gm.) at birth. He was entirely breast fed for only three weeks and partially breast fed for six months, at which age he weighed 17 pounds and 10 ounces (7.9 Kg.). His feeding history was uneventful. At the age of 1 year, he weighed approximately 24 pounds (10.9 Kg.). He experienced minor upper respiratory infections and was vaccinated successfully (Nov. 28, 1923). He received cod liver oil early, but was slow in dentition and walking. At 22 months, he weighed 29 pounds (13.2 Kg.). A urinalysis at this time (March 27, 1924) was entirely negative.

When seen on April 14, 1925, the boy weighed 30 pounds and 7 ounces (13.8 Kg.). He was said to have weighed 32 pounds and 8 ounces (14.7 Kg.) on the household scales the preceding fall. On April 1, he had been attended by one of us (D. J. L.) for a mild griplike infection. Pallor and loss of weight had occurred subsequent to this illness. On examination, except for the pallor, evident weakness, loss of weight and signs of moderate rickets, the observations were negative. There was no history of polyuria, polyphagia or polydipsia. The reduction of Fehling's solution by the urine, however, was pronounced. The Fehling test, on standing, gave a heavy yellow precipitate, and Benedict's quantitative test showed 5 per cent of reducing substance present.

On April 15, 50 cc. of the urine was tested as to fermentability, with baker's yeast and with two controls, one of 1 per cent glucose solution, and the other of normal urine. On April 16, only the glucose solution was fermented, whereas on the following day both the glucose solution and the patient's urine showed gas bubbles. Because of these results, tests for pentose were made (Bial's and Tollen's),[2] and this sugar was discovered to be present.

However, since on April 16, the blood sugar when fasting (Harper Hospital laboratory) was 0.143 Gm. per hundred cubic centimeters, insulin (5 units three times a day) in conjunction with a diabetic diet was started, with no untoward results until April 19, when the child had a reaction three hours after injection in the evening. Consequently, the amount of insulin was reduced, and it was discontinued entirely on April 27. It is an interesting and perhaps significant fact that the boy gained 1 pound and 11 ounces (765 Gm.) during the eleven days of this regimen.

On May 15, the observations on the blood sugar were as follows: One hour before breakfast, 0.095 Gm.; one hour after breakfast, 0.095 Gm.; three hours after breakfast, 0.095 Gm. The diet was therefore gradually increased (with frequent checks on the urine) until at the present time there are no restrictions based on the urinary condition. He has, in the meantime, undergone several minor febrile upper respiratory infections, with prompt and uncomplicated recovery and no apparent after-effect, and particularly with no reappearance of glucose in the urine. Pentose, however, in practically unvarying amount continues to be present.

*Laboratory Observations.*—In the study of this case, the following reactions,[2] said to be typical of pentose, were obtained: (1) a green precipitate when the urine was layered over boiling Bial's reagent; (2) a red color when the urine was boiled on the water bath with hydrochloric acid and phloroglucin; (3) yellow, needle-like phenylosazone crystals (purified by repeated recrystallizations from hot 10 per cent alcohol) melting at 156 C.; (4) negative fermentation tests with yeast.

Through the courtesy of Dr. Aldo Castellani,[3] cultures of *Monilia tropicalis, Monilia krusei* (Cast.), *Bacillus paratyphosus B.* and *Bacillus coli-communis* were obtained, and fermentation tubes of the urine and

2. Hawk, Philip: Practical Physiological Chemistry, Philadelphia, P. Blakiston's Son & Company, 1918.

3. Castellani, A., and Taylor, F. E.: Fallacies of "Yeast Method" of Detecting Glucose in Urine, J. A. M. A. **86**:523 (Feb. 20) 1926.

controls were inoculated. The results were negative throughout, possibly due to the fact that the sugar was present in such small amounts.

The nature of the metabolic disturbance present is a matter of speculation. Alexander [4] reported a case in a boy, aged 18 months, in whom pentose disappeared from the urine when milk was eliminated from the diet. In Aron's [5] case (a 5 year old boy), the output of pentose was wholly independent of the nature of the food taken. In our patient, also, the amount of pentose had no relation to the diet. Since May 19, 1925, quantitative analyses with Benedict's solution have shown amounts constantly ranging from 0.071 to 0.625 Gm. per hundred cubic centimeters, 75 per cent of the determinations giving approximately 0.2 Gm. per hundred cubic centimeters. Attempts to increase the demonstrable amount of pentose by boiling the urine with acid before performing the Fehling test have been unsuccessful. (The theory of Neuberg [6] is that the pentose is partly in combination in the urine as a ureid).

Seliwanoff's [7] test for sugars of the ketone group was positive in fourteen of twenty-two specimens. The tests for urobilin, urobilinogen, indican, lactose and galactose were uniformly negative. Acetone was found several times. The twenty-four-hour volume of urine has varied from 750 cc. to 1,570 cc., averaging 1,177 cc. Holt [8] gives the average for a child of 2 to 5 years as 500 to 800 cc. The specific gravity of twenty specimens ranged from 1.008 to 1.034, averaging 1.021. Examination of blood smears and of the stool were not enlightening; in particular, the apparent fat content of the stool was not increased. Bial's test of the blood serum was positive.

The type of pentose present was not determined. A single specimen examined with the polariscope was optically inactive. Seliwanoff's reaction was not constantly present, so that the sugar is probably not a ketopentose, but an aldopentose, the group of sugars to which arabinose belongs.

The question arises as to whether the first finding of 5 per cent of sugar was accurate. Against it is the fact that the following determinations were all decidedly lower. In favor of it is the blood sugar observation of April 16, which was certainly a high normal, the fact that the early doses of insulin did not produce shock, and the child's improvement under a diabetic regimen. It is possible also that when first seen,

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4. Alexander, Alfred: Pentosurie and Darmstörung, Arch. f. Verdauungskr. **24**:286, 1918.

5. Aron, Hans: Ein Fall von Pentosurie im frühen Kindesalter, Monatschr. f. Kinderh. **12**:177, 1913.

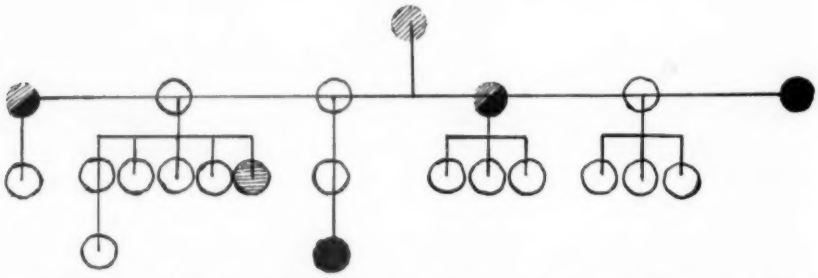
6. Von Noorden, Carl: Handbuch der Pathologie des Stoffewechsels, Berlin **2**:220, 1907.

7. Browne, C. A.: A Handbook of Sugar Analysis, New York, John Wiley & Sons, 1912, p. 380.

8. Holt, L. E., and Howland, John: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1922, p. 592.

he may have had an alimentary glycosuria. In other instances of pentosuria recorded,[1] transitory glycosuria has been present. In the case of one aunt and one uncle of the child, both of whom show persistent pentosuria, glucose is demonstrable occasionally.

The family occurrence of pentosuria, which has been a matter of frequent observation, is well instanced in this case, as pentose has been demonstrated in three other members of the family, including a granduncle and two grandaunts, both on the maternal side. The maternal great-grandmother (who died in 1914) also was known to have had a reducing substance in her urine which was considered at the time to be glucose. A slight trace of sugar in the urine of a second cousin recently operated on for appendicitis was reported in a preoperative analysis. This condition could not be confirmed subsequently, and a determination of the blood sugar made during the convalescence was normal.



Schema showing reducing substances present in urine in four generations of family; white circles, no reducing substance in urine; circle with diagonal lines, reducing substance, probably glucose; black circles, pentose; circles one half diagonal, one-half black lines, glucose and pentose; circle with horizontal lines, transitory reducing substance.

Besides the patient whose history is here recorded, there is only one other member of the fourth generation of the family, an infant who at 12 months of age showed a normal urine. Of thirteen members of the third generation, the urine has been examined in the case of all, with negative observations (unless the reducing substance in the preoperative case just referred to is significant). In the generation of the patient's grandmother, there are three known cases of pentosuria, and the great-grandmother had a sugar in her urine, thought to have been glucose.

According to Garrod,[1] inborn errors of metabolism "are wont to occur in several members of a family, most often in brothers and sisters whose parents do not share their peculiarity, and whose children also, are usually immune." He cites statistics covering the occurrence of the commoner anomalies of metabolism, demonstrating the preponderance of such incidence in males. A consideration of the recorded cases of pentosuria suggests a fairly definite law governing its transmission. It would be interesting to study this occurrence from a mendelian standpoint.

COMMENT

The case of essential pentosuria herein described presents the following points of interest:

1. It shows the necessity of careful chemical investigation of the urine and the blood before administering insulin.

2. It presents a type of hereditary anomaly. The case is that of the youngest patient on record, and tends to support the supposition that the pentosuria is present from birth, although a single specimen examined some months before the pentosuria was recognized was negative. The familial character of the disturbance accords with other recorded instances.

3. It raises speculation as to the nature of the metabolic disorder present. The source of the pentose in this case was not the diet, because (with the exception of the first analysis of the urine) the amount of pentose has been remarkably constant in spite of dietary variations. Thus ten specimens examined from July 25 to August 17, 1925, contained the following percentages of pentose (calculated as glucose): 0.24, 0.209, 0.185, 0.209, 0.178, 0.2, 0.209, 0.208, 0.172, 0.263. Levene and LaForge [9] found in their case that the urine contained only 0.25 per cent of the pentose. In a case of Hiller's,[10] the concentration varied between 0.1 and 0.3 per cent.

The narrow limits in which the output of pentose has fluctuated is interesting, and suggests a comparison with the uniformity of the amounts of cystine excreted in cystinuric subjects. Garrod [1] has published a table of quantitative analyses of specimens of urine of cystinuric patients made by different investigators with various methods, and has shown that the excretion of this substance is remarkably constant, varying from 0.3 to 0.5 Gm. in twenty-four hours. Garrod assumes the uniformity to be due to the failure of the body to utilize in its usual way some definite part of the protein metabolized.

4. The relationship of pentosuria to diabetes mellitus cannot be dismissed lightly. In this case the pallor and loss of weight following an acute infection might lead one to suspect the existence of a true diabetes. Moreover, there was an unusually large output of urine. Furthermore, the child improved on a diabetic diet, together with the administration of insulin.

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9. Levene, P. A., and LaForge, F. B.: Note on a Case of Pentosuria, J. Biol. Chem. **15**:481, 1913.

10. Hiller, Alma: The Identification of the Pentose in a Case of Pentosuria, J. Biol. Chem. **30**:129, 1917.

# EPILEPSY

## CHEMICAL INVESTIGATIONS OF RATIONAL TREATMENT BY PRODUCTION OF KETOSIS *

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The study of the treatment of epilepsy was undertaken by the children's service at the Massachusetts General Hospital in 1921, and has been carried on through various stages to date. The first stage in this work consisted in the study of fasting epileptic children, and the determination of the clinical and the chemical results of such fasting. In all, twenty-four children fasted. Ten of these patients were studied chemically, and the reports on the results in the first eight appear in articles by Hoeffel and Moriarty [1] and Shaw and Moriarty,[2] while cases 9 and 10 are reported in table 1.

Clinically, the convulsive attacks stopped in all of these children during the fast. Although there was a temporary cessation of attacks following the fast, in all cases the attacks recurred after varying intervals of freedom.

The last two cases, recorded in table 1, showed essentially the same results as were observed in the earlier patients.

The outstanding conclusions from the study of the effect of fasting on epilepsy are: During fasting the epileptic attacks are stopped; some time after the fast is broken they recur again; during fasting there is an increased blood uric acid concentration; a lowering of the blood sugar, a slight lowering of the $p_H$ of the blood, diminution of the carbon dioxide combining power and a marked excretion of acetone bodies, shown qualitatively in the breath and urine. It was also seen in these cases that there was no change in the blood nonprotein nitrogen and amino-acids.

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* Received for publication, Sept. 17, 1926.

* From the Children's Medical Department, Massachusetts General Hospital, and the Department of Pediatrics, Harvard Medical School.

1. Hoeffel, G. N., and Moriarty, M. E.: The Effects of Fasting on the Metabolism of Epileptic Children, Am. J. Dis. Child. **28**:16 (July) 1924.

2. Shaw, E. B., and Moriarty, M.: Hypoglycemia and Acidosis in Fasting Children with Idiopathic Epilepsy, Am. J. Dis. Child. **28**:553 (Nov.) 1924.

The beneficial results of fasting at this stage were attributed largely to the acidosis produced. The work of Jarloev [3] and Geyelin [4] substantiated this idea. The production of a ketosis at this time was considered a coincident change of minor importance.

Potassium borotartrate had been highly recommended by Pierre Marie and his co-workers [5] in the treatment of epilepsy. Marie attributed the benefit which he claimed to the boron in the compound. In the belief that this reported benefit might be due to the acid radical and not to the boron in the salt, the drug was administered to patients in this clinic over a period of several months but without affecting the epileptic symptoms. The chemical tests carried out in fasting

TABLE 1.—*Chemical Observations During Fast*

| | Controls Before Fast | Days of Fast | | | | | | | | | Fifth Day After Food Was Given |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
| Uric Acid,* Mg. per 100 Cc. | | | | | | | | | | | |
| Case 9, S. G..... | 2.92 | .. | 3.92 | .. | .... | .. | 5.72 | .. | 5.72 | 4.52 | 1.62 |
| Case 10, W. C..... | 2.08 | .. | 5.40 | .. | 4.52 | .. | 5.32 | .. | 7.60 | 4.84 | 1.92 |
| Breath Acetone,† appearance time in seconds | | | | | | | | | | | |
| S. G..... | Absent | .. | 35 | .. | 25 | .. | 20 | .. | 18 | 15 | Absent |
| W. C..... | Absent | .. | 20 | .. | 15 | .. | 10 | .. | 10 | 7 | Absent |
| Alkali Reserve,‡ $CO_2$ combining power per cent by volume | | | | | | | | | | | |
| S. G.....53.2, | 58.6, 62.1 | .. | 40.2 | .. | 48.7 | .. | 41.2 | .. | 41.3 | 49.8 | 61.5 |
| W. C..... | 59.2 | .. | 38.7 | .. | 36.5 | .. | 44.2 | .. | 38.2 | 41.8 | .... |
| Blood Sugar,§ Mg. per 100 Cc. | | | | | | | | | | | |
| S. G..... | 98, 91 | .. | 80 | .. | 67 | .. | 78 | .. | 78 | 39# | 84 |
| W. C..... | 79, 84 | . | 51 | .. | 54 | .. | 81 | .. | .. | 69 | 83 |

* Folin, O., and Wu, H.: J. Biol. Chem. **38**: 81 [May] 1919.
† Shaw, E. B., and Moriarty, M.: Am. J. Dis. Child. **28**: 553 [Nov.] 1924.
‡ Van Slyke, D. D.: J. Biol. Chem. **30**: 347 [June] 1919.
§ Folin, O., and Wu, H.: J. Biol. Chem. **41**: 367 [March] 1920.
# Fever from respiratory infection.

patients were repeated in the patients who were given potassium borotartrate, and they failed to show that the drug, even in large doses, caused any chemical changes in the constituents examined.

Since a ketosis-acidosis was marked during fasting while the patients were free from attacks, it was considered that the ketosis might be the factor responsible for the good therapeutic results obtained. It was clinically impractical to keep a child in a state of ketosis by fasting for more than a few days, so it became evident that a way of maintaining a ketosis over a long period of time would have to be devised. A dietetic

3. Jarloev, E.: Compt. rend. Soc. de biol. **84**:156, 1921.
4. Geyelin, H. R.: Med. Rec. **99**:1037, 1921.
5. Marie; Crouzon, and Bouttier: Potassium Borotartrate in Treatment of Epilepsy, Bull. Acad. de méd., Paris **83**:504 (June) 1920; Presse méd. **28**:713 (Oct.) 1920.

method for doing this was worked out by Wilder [6] and later by Peterman.[7] It was found possible to arrange a diet so that a child could be kept in a state of ketosis over a long period of time, for weeks, months or even years. This was accomplished by so apportioning the food that the ketogenic outbalanced the antiketogenic elements of the diet. If the relationship of the ketogenic foods to the antiketogenic foods is 1.5 : 1, ketosis does not develop. With an increase of this ratio to 2 : 1 or more, a ketosis develops, and the higher the ratio the greater is the ketosis. Coincidentally with the marked ketonuria resulting from diets of higher ketogenic ratios, a reduction or cessation of attacks has occurred.[8]

A series of children with epilepsy have been treated by ketogenic diet and studied, both clinically and chemically, during the past two years. It was found that symptomatic cure could be expected in at least 30 per cent of the patients when the diet was accurately followed. The chemical observations on the blood in seventeen cases are given in table 2.

The important conclusion that can be drawn from this table is that the same chemical changes are obtained on a highly ketogenic diet as during the fast, but usually to a less degree. Table 2 shows that as the carbohydrate in the food is reduced and the fat is increased, there results an increasing production of acetone [9] in the blood. Associated with the acetone production there is a diminution in the amount of sugar found in the blood. The blood sugar in fasting children is generally between 50 and 70 mg. per hundred cubic centimeters, while in children on a ketogenic diet, it is somewhat higher, between 60 and 80 mg. per hundred cubic centimeters. The carbon dioxide combining power in children during fasting varies between 35 and 45 per cent by volume, while on a ketogenic diet the average carbon dioxide combining power of the blood is from 40 to 50 per cent by volume. The blood uric acid showed

6. Wilder, R. M.: The Effects of Ketonuria on the Course of Epilepsy, Mayo Clinic Bull. **2**:307, 1921.

7. Peterman, M. G.: The Ketogenic Diet in the Treatment of Epilepsy, Am. J. Dis. Child. **28**:28 (July) 1924.

8. In this clinic, the diet ratio has been based on the relationship of the food constituents themselves (a ratio which for the most part approximates the Woodyatt fatty acid to glucose ratio of ketogenic to antiketogenic constituents). Thus, a 1.5 : 1 ratio means that the diet contains 1.5 Gm. of fat for each gram of carbohydrate and protein (combined). The amounts of food constituents for a given ratio are calculated from the two facts represented in the following equations, always remembering that the protein allowance for any patient is 1 Gm. for each kilogram of the patient's expected body weight. The total caloric needs are 50 per cent above the basal requirements. (Talbot, F. B.: Physiol. Rev. **5**:477 [Oct.] 1925). By "ratio" in the following equations is meant 1.5 in a 1.5 : 1 diet, 2 in a 2 : 1 diet, etc. (Gm.) Fat = ratio (Gm. Carbohydrate + Gm. Protein). Total calories = $9 \times$ [Ratio (C + P)] + 4 C + 4 P.

9. Van Slyke, D. D.: Studies of Acidosis: VIII. Acetone Bodies in the Blood, J. Biol. Chem. **32**:495 (Dec.) 1917.

| Case | Diet Ratio | Days on Ratio | Diet | | | Blood Chemistry | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Carbohydrate, Gm. | Protein, Gm. | Fat, Gm. | Carbon Dioxide Combining Power Plasma, per Cent by Volume | Sugar Whole Blood, Mg. per 100 Cc. | Acetone Whole Blood, Gm. per Liter | Uric Acid Whole Blood, Mg. per 100 Cc. | Nonprotein Nitrogen Whole Blood, Mg. per 100 Cc. | Phosphorus Plasma, Mg. per 100 Cc. | Calcium Plasma, Mg. per 100 Cc. | Chlorides Whole Blood, Mg. per 100 Cc. |
| R. R. ..... | 2:1 | 2 | 43.5 | 27 | 141 | 45.6 | 74 | ..... | 3.60 | 35 | .... | 12.4 | ... |
| 7 years | 3:1 | 78 | 23 | 27 | 150 | 47.4 | 72 | 0.342 | 4.27 | 32.6 | 3.18 | .... | ... |
| E. J. ..... | 3:1 | 7 | 20 | 25 | 135 | .... | 64 | ..... | 5.4 | 35 | .... | .... | ... |
| 7½ years | 3:1 | 32 | 20 | 25 | 135 | 45.8 | 66 | 0.259 | 4.95 | 25.6 | 2.56 | .... | 496 |
| J. S. ..... | 3:1 | 35 | 25 | 27 | 155 | 53.2 | 78 | ..... | 4.64 | 41.5 | 4.4 | 9.2 | 416 |
| 7 years | 3:1 | 154 | 25 | 27 | 155 | 43.3 | 72 | 0.218 | 5.27 | 27.5 | 2.42 | 10.0 | 478 |
| S. G. ..... | House diet | .. | .. | .. | ... | 53.2 | 98-137 | | | | | | |
| | | | | | | | 161-143 | ..... | 2.92 | 23.4 | .... | .... | ... |
| | 1.3:1 | 1 | 51 | 41 | 121 | 58.6 | 80 | ..... | 2.16 | 28.0 | .... | .... | ... |
| | 1.3:1 | 8 | 51 | 41 | 121 | 62.1 | 91 | ..... | .... | .... | .... | .... | ... |
| | 4:1 | 3 | 6 | 30 | 148 | .... | 68 | ..... | 2.56 | .... | .... | .... | ... |
| | 4:1 | 6 | 6 | 30 | 148 | 50.1 | 82 | ..... | 2.40 | .... | .... | .... | ... |
| | 4:1 | 8 | 6 | 30 | 148 | 50.1 | .. | ..... | .... | .... | .... | .... | ... |
| | 4:1 | 11 | 6 | 30 | 148 | 53.0 | .. | ..... | .... | 23.4 | .... | .... | ... |
| | 4:1 | 13 | 6 | 30 | 148 | 51.8 | 86 | 0.762 | 2.64 | .... | .... | .... | ... |
| | 4:1 | 16 | 6 | 30 | 148 | 57.7 | 85 | 0.839 | .... | 31.0 | .... | .... | ... |
| W. C. ..... | House diet | .. | .. | .. | ... | .... | 79-122 | | | | | | |
| | | | | | | | 129-108 | ..... | 2.08 | 26.0 | .... | .... | ... |
| | 1.5:1 | 8 | 52 | 42 | 122 | 59.2 | 84 | ..... | .... | .... | .... | .... | ... |
| | 4:1 | 2 | 6 | 30 | 148 | 40.3 | 57 | ..... | 4.08 | .... | .... | .... | ... |
| | 4:1 | 3 | 6 | 30 | 148 | 43.5 | 63 | ..... | 4.04 | .... | .... | .... | ... |
| | 4:1 | 4 | 6 | 30 | 148 | 43.7 | .. | ..... | 2.08 | .... | .... | .... | ... |
| E. G. ..... | House diet | .. | .. | .. | ... | 52.5 | 74-146 | | | | | | |
| | | | | | | | 162-123 | ..... | 3.40 | 30.0 | .... | .... | ... |
| | 2:1 | 12 | 44 | 40 | 168 | 50.8 | 65 | ..... | .... | 30.0 | 5.94 | 10.2 | 679 (plasma) |
| | 2:1 | 20 | 44 | 40 | 168 | 48.3 | 75 | ..... | 3.92 | 26 | .... | .... | 625 (plasma) |
| | 3:1 | 11 | 20 | 40 | 180 | 54.7 | 75 | 0.268 | 3.84 | 28.8 | .... | 12.5 | ... |
| | 4:1 | 23 | 6 | 40 | 184 | 50.9 | 81 | 0.572 | 4.76 | .... | 3.87 | 10.7 | ... |
| | 4:1 | 34 | 6 | 40 | 184 | 46.8 | 76 | ..... | 4.56 | 22.8 | .... | .... | ... |
| C. C. ..... | 3:1 | 17 | 21 | 50 | 213 | 48.8 | 71 | 0.411 | .... | .... | 4.0 | 8.7 | ... |
| E. G. ..... | 3:1 | 9 | 20 | 40 | 180 | 44 | 76 | 0.576 | 3.24 | 39 | 3.7 | 11.0 | 467 |
| | 5:1 | 3 | 3 | 35.5 | 190 | 46 | 62 | 0.935 | 5.16 | 29 | 3.99 | 11.13 | 426 |
| | 1:6 | 2 | 296 | 40 | 56 | 54.1 | 64 | 0.144 | 4.16 | 22.6 | .... | .... | ... |
| | 1:6 | 4 | 296 | 40 | 56 | 58.9 | 62 | 0.052 | .... | 23 | 2.82 | .... | ... |
| | 1:6 | 5 | 296 | 40 | 56 | .... | 93 | ..... | 4.24 | .... | .... | .... | ... |
| F. M. ..... | House diet | .. | .. | .. | ... | 52.8 | 85 | ..... | 4.01 | .... | .... | .... | 433 |
| 7 years | 1.5:1 | 4 | 58 | 22 | 120 | .... | .. | ..... | .... | .... | 3.12 | 11.9 | ... |
| | 2:1 | 2 | 42 | 22 | 129 | .... | 69 | 0.731 | .... | .... | .... | 11.2 | ... |
| B. S. ..... | House diet | .. | .. | .. | ... | 47.7 | 82 | ..... | .... | .... | .... | .... | ... |
| 3½ years | 4:1 | 3 | 125 | 15 | 110 | 45.9 | 73 | ..... | .... | .... | .... | .... | ... |
| | 3:1 | 105 | 20.5 | 15 | 106.5 | 41.2 | 78 | ..... | 4.4 | 30.1 | 2.9 | .... | 501 |
| W. H. ..... | 3:1 | 17 | 21 | 21 | 126 | .... | 69 | ..... | 3.64 | 33 | .... | .... | ... |
| 6 years | 3:1 | 23 | 21 | 21 | 126 | 46.1 | .. | 0.533 | .... | 39 | 3.2 | 11.1 | 450 |
| | 3:1 | 27 | 21 | 21 | 126 | 43.0 | 71 | ..... | 3.08 | .... | .... | .... | ... |
| E. A. ..... | House diet | .. | .. | .. | ... | 58.2 | 94 | 0.076 | 3.60 | 32 | 3.18 | 10.4 | 449 |
| 11 years | 3:1 | 2 | 21 | 37 | 174 | 45.3 | 78 | 0.071 | 5.60 | 33 | 3.4 | .... | 446 |
| | 3.5:1 | 4 | 14 | 37 | 178 | .... | .. | 0.345 | .... | .... | 4.0 | 10.3 | 499 |
| | 3.5:1 | 8 | 14 | 37 | 178 | 47.1 | 70 | 0.343 | 6.04 | 30 | .... | .... | ... |
| J. P. ..... | 2:1 | 5 | 25 | 37 | 73 | 41.9 | 61 | ..... | 3.4 | 29.1 | 3.2 | 10.4 | 487 |
| 2 years | | | | | | | | | | | | | |
| P. H. ..... | 3:1 | 16 | 11 | 60 | 213 | 47 | 79 | 0.535 | 3.28 | 28.0 | 2.5 | 11.9 | 459 |
| 15 years | | | | | | | | | | | | | |
| J. B. ..... | House diet | .. | .. | .. | ... | 53.3 | 99 | ..... | 4.6 | 32 | 3.7 | .... | 487 |
| 12 years | 3:1 | 17 | 22 | 41 | 189 | 45.2 | 67 | 0.450 | 4.56 | 28 | 2.42 | 11.9 | 469 |
| E. G. ..... | 1:2 | .. | 177 | 40 | 109 | 56.1 | 95 | ..... | .... | .... | .... | .... | ... |
| 12 years | 4:1 | 7 | 6 | 40 | 184 | 41.7 | 68 | 0.599 | .... | 32 | 2.9 | .... | 473 |

TABLE 3.—*Urinary Excretion of Total Acetone Bodies on Ketogenic Diets.*

| | Age, Years | Diet Ratio | Diet: Carbohydrate, Gm. | Diet: Protein, Gm. | Diet: Fat, Gm. | Days on Ratio | Urine Volume, Cc. | Acetone Bodies: Concentration, Gm./Liter | Acetone Bodies: Total, Gm. |
|---|---|---|---|---|---|---|---|---|---|
| E. G. | 12 | 1.5:1 | 66 | 40 | 159 | 3 | 2,520 | 0.213 | 0.324 |
| | | | | | | 4 | 2,500 | 0.274 | 0.685 |
| | | 2:1 | 44 | 40 | 168 | 1 | 2,385 | 0.312 | 0.746 |
| | | | | | | 2 | 2,730 | 1.018 | 2.780 |
| | | | | | | 3 | 2,080 | 1.652 | 3.438 |
| | | | | | | 4 | 2,300 | 0.545 | 1.254 |
| | | 3:1 | 20 | 40 | 180 | 1 | 2,250 | 2.532 | 5.695 |
| | | | | | | 2 | 2,350 | 2.917 | 6.855 |
| | | | | | | 3 | 2,125 | 5.265 | 11.961 |
| | | 4:1 | 6 | 40 | 184 | 1 | 2,640 | 4.744 | 12.524 |
| | | | | | | 2 | 2,650 | 2.355 | 6.340 |
| | | | | | | 3 | 2,600 | 0.538 | 1.400 |
| | | | | | | 4 | 2,560 | 0.935 | 2.394 |
| | | | | | | 5 | 2,260 | 1.143 | 2.583 |
| | | | | | | 7 | 2,565 | 1.980 | 5.069 |
| | | | | | | 8 | 1,880 | 3.314 | 6.270 |
| R. R. | 7 | 3:1 | 23 | 27 | 150 | 46 | 1,000 | 3.079 | 3.079 |
| J. S. | 22 | 3.5:1 | 12 | 39 | 181 | 74 | 740 | 5.424 | 4.014 |
| O. B. | 9 | 3.5:1 | 14½ | 29 | 152 | 11 | 1,040 | 3.967 | 4.127 |
| C. C. | 13 | 2.3:1 | 46 | 51 | 224 | 8 | 1,350 | 4.627 | 6.251 |
| | | | | | | 21 | 960 | 3.242 | 3.072 |
| | | 3:1 | 21 | 50 | 213 | 8 | 1,020 | 7.483 | 7.633 |
| | | | | | | 27 | 1,140 | 5.288 | 6.028 |
| | | | | | | 50 | 960 | 5.800 | 5.568 |
| | | | | | | 66 | 1,440 | 1.995 | 2.872 |
| | | | | | | 119 | 1,170 | 3.678 | 4.303 |
| W. H. | .. | 3:1 | 21 | 21 | 126 | 20 | 720 | 3.194 | 2.297 |
| | | | | | | 21 | 1,620 | 6.158 | 9.979 |
| | | | | | | 22 | 880 | 2.212 | 1.945 |
| | | | | | | 23 | 1,010 | 3.474 | 3.505 |
| | | | | | | 24 | 820 | 4.766 | 3.911 |
| | | 3.5:1 | 16 | 21 | 130 | 1 | 815 | 5.170 | 4.249 |
| E. J. | 7½ | 3:1 | 20 | 25 | 135 | 2 | 340 | 13.399 | 4.556 |
| | | | | | | 4 | 840 | 10.473 | 8.796 |
| | | | | | | 6 | 1,645 | 2.283 | 3.767 |
| | | | | | | 7 | 2,260 | 0.817 | 1.847 |
| | | | | | | 8 | 1,260 | 2.464 | 3.105 |
| | | | | | | 9 | 535 | 8.223 | 4.319 |
| B. S. | 3½ | 1.5:1 | 48 | 15 | 94 | 2 | 200 | 1.794 | 0.358 |
| | | | | | | 4 | 475 | 0.456 | 0.219 |
| | | | | | | 5 | 500 | 1.120 | 0.560 |
| | | | | | | 6 | 380 | 1.442 | 0.548 |
| | | 2:1 | 35 | 15 | 100 | 1 | 280 | 2.507 | 0.703 |
| | | | | | | 2 | 240 | 4.386 | 1.054 |
| | | | | | | 3 | 320 | 5.135 | 1.642 |
| | | | | | | 6 | 360 | 3.794 | 1.364 |
| | | 3:1 | 20.5 | 15 | 106½ | 2 | 635 | 3.483 | 2.211 |
| | | | | | | 3 | 880 | 2.972 | 2.615 |
| | | | | | | 9 | 870 | 5.006 | 4.354 |
| | | | | | | 10 | 630 | 3.358 | 2.115 |
| | | | | | | 14 | 455 | 3.452 | 1.571 |
| | | 4:1 | 12.5 | 15 | 110 | 3 | 400 | 5.023 | 2.009 |
| | | | | | | 4 | 640 | 5.398 | 3.455 |
| | | | | | | 5 | 600 | 4.984 | 2.990 |
| | | | | | | 6 | 1,170 | 3.317 | 3.881 |
| | | | | | | 7 | 680 | 4.310 | 2.931 |
| J. S. | 7 | 3.5:1 | 18 | 27 | 158 | 61 | 440 | 5.846 | 2.574 |
| | | | | | | 85 | 630 | 3.517 | 2.216 |

TABLE 3.—*Urinary Excretion of Total Acetone Bodies on Ketogenic Diets—Continued*

| | Age, Years | Diet Ratio | Diet: Carbohydrate, Gm. | Diet: Protein, Gm. | Diet: Fat, Gm. | Days on Ratio | Urine Volume, Cc. | Acetone Bodies: Concentration, Gm./Liter | Acetone Bodies: Total, Gm. |
|---|---|---|---|---|---|---|---|---|---|
| E. G. | 12 | 3:1 | 20 | 40 | 180 | 1 | 1,500 | 1.245 | 1.860 |
| | | | | | | 2 | 1,370 | 1.616 | 2.206 |
| | | | | | | 3 | 1,920 | 2.022 | 3.838 |
| | | | | | | 4 | 2,030 | 3.664 | 8.430 |
| | | | | | | 5 | 2,030 | 3.456 | 7.024 |
| | | 4:1 | 6 | 40 | 184½ | 1 | 2,850 | 3.471 | 8.890 |
| | | | | | | 4 | 1,615 | 7.234 | 11.568 |
| | | | | | | 5 | 2,460 | 3.780 | 9.599 |
| | | | | | | 6 | 2,000 | 7.614 | 15.226 |
| | | | | | | 7 | 2,460 | 2.397 | 5.904 |
| | | | | | | 8 | 1,960 | 6.108 | 12.956 |
| | | | | | | 9 | 1,530 | 7.070 | 10.817 |
| | | 5:1 | 3 | 37½ | 190 | 1 | 1,660 | 9.851 | 16.351 |
| | | | | | | 2 | 1,200 | 7.720 | 9.273 |
| | | | | | | 3 | 1,580 | 9.540 | 15.076 |
| P. H. | 15 | 3:1 | 11 | 60 | 213 | 7 | 1,400 | 3.223 | 4.512 |
| | | | | | | 16 | 820 | 4.307 | 3.528 |
| | | | | | | 95 | 840 | 3.231 | 2.714 |
| A. H. | 12½ | 2:1 | 44 | 40 | 168 | 7 | 640 | 0.823 | 0.531 |
| | | 3:1 | 20 | 40 | 168 | 18 | 880 | 7.352 | 6.468 |
| E. A. | 11 | 3.5:1 | 14 | 37 | 146 | 2 | 1,430 | 1.900 | 2.717 |
| | | | | | | 3 | 1,630 | 2.635 | 4.295 |
| | | | | | | 4 | 1,520 | 3.793 | 3.665 |
| | | | | | | 9 | 1,860 | 1.333 | 2.479 |
| J. B. | 12 | 1.5:1 | 66 | 40 | 158 | 1 | 940 | 0.218 | 0.205 |
| | | | | | | 2 | 1,210 | 0.110 | 0.133 |
| | | | | | | 3 | 1,990 | 0.111 | 0.211 |
| | | 2:1 | 48 | 41 | 177 | 5 | 1,205 | 3.284 | 3.974 |
| | | 3:1 | 22 | 41 | 189 | 1 | 2,485 | 1.654 | 4.704 |
| | | | | | | 2 | 2,510 | 3.444 | 8.644 |
| | | | | | | 4 | 2,190 | 2.980 | 6.506 |
| | | | | | | 6 | 1,480 | 5.705 | 8.443 |
| | | | | | | 7 | 1,480 | 3.221 | 4.967 |
| | | | | | | 11 | 1,465 | 2.757 | 4.053 |
| | | | | | | 13 | 1,400 | 5.217 | 7.304 |
| | | 3:1 | 14.5 | 50 | 190½ | 2 | 2,470 | 2.924 | 7.242 |
| S. B. | 7 | 3:1 | 20 | 32 | 162 | 4 | 1,790 | 1.822 | 3.261 |
| | | | | | | 10 | 2,280 | 3.088 | 7.041 |

similar changes to those found during fasting, but to a less degree. There is no marked change in the nonprotein nitrogen,[10] phosphorus,[11] calcium [12] or chlorides.[13]

Determinations of the urine acetone bodies [14] resulting from various ketogenic diets were made on a series of patients in the hospital and in the outpatient department. These results are shown in table 3.

10. Folin, O., and Wu, H.: System of Blood Analysis, J. Biol. Chem. **38**:81 (May) 1919.

11. Briggs, A. P.: Modification of the Bell-Doisey Method for Phosphorus Determination, J. Biol. Chem. **53**:13 (July) 1922.

12. Clark, E. P., and Collip, J. B.: Modification of the Tisdall Method for Calcium, J. Biol. Chem. **63**:461 (March) 1925.

13. Van Slyke, D. D.: Determination of Chlorides in Blood and Tissues, J. Biol. Chem. **58**:523 (Dec.) 1923.

14. Van Slyke, D. D.: Studies of Acidosis: VII. Acetone Bodies in the Urine, J. Biol. Chem. **32**:455 (Dec.) 1917.

The excretion of acetone increases rapidly as the ketogenic ratio is increased. Qualitative acetone and diacetic acid tests of the urine, as well as the acetone test of the breath, give a good index as to whether the diet is being followed or not, but give no measure of the large amounts of total acetone bodies present in the urine. Table 3 shows that as much as 16 Gm. was excreted in one day. In some cases there seemed to be a peak of ketone excretion which was not found again even with increased ratios. The excretion of acetone bodies varied between 2 and 6 Gm. on the higher ketogenic diets followed at home.

The quantities of excreted acetone are compared only with ratios of the ingested food, since it did not seem feasible to obtain respiratory quotients on these children and in that way determine the ratio of the metabolized food.

TABLE 4.—*The Effect of Carbohydrate on Ketone Formation as Shown by Excretion of Acetone Bodies in Breath, Blood and Urine. Total Acetone Bodies Calculated as Acetone.*

| | Diet | | | Urine, 24 Hour Specimen, Gm. (Normal, 0.420) | Breath, Fasting, Appearance Time in Seconds (Normal, Absent) | Blood, Fasting, Gm. per Liter (Normal, 0.013-0.026) | Attacks (Before Diet, 40-80 Daily) |
|---|---|---|---|---|---|---|---|
| | Carbohydrate, Gm. | Protein, Gm. | Fat, Gm. | | | | |
| On high fat diet... | 3 | 35 | 190 | 16.35 | 6 | ..... | 0 |
| | 3 | 35 | 190 | 9.27 | 6 | ..... | 0 |
| | 3 | 35 | 190 | 15.07 | 5 | 0.935 | 0 |
| On high carbohydrate diet | | | | | | | |
| First 24 hours... | 296 | 40 | 56 | 1.88 | 140 | ..... | 0 |
| Second 24 hours. | 296 | 40 | 56 | 0.65 | 210 | 0.144 | 0 |
| Third 24 hours... | 296 | 40 | 56 | 0.46 | Absent | ..... | 0 |
| Fourth 24 hours. | 296 | 40 | 56 | 0.80 | Absent | 0.052 | 1 |
| Fifth 24 hours... | 296 | 40 | 56 | 0.90 | Absent | ..... | 1 |
| Sixth 24 hours... | 296 | 40 | 56 | 0.32 | Absent | ..... | 6 |
| Seventh 24 hours | 296 | 40 | 56 | 0.22 | Absent | ..... | 7 |
| | | | | | | | 33 attacks by eleventh day |

The addition of carbohydrates to the diet causes the acetone in the urine, breath and blood to disappear rapidly.

The excessive amounts of acetone disappeared from the urine, breath and blood within twenty-four to forty-eight hours after the change to any ordinary home diet. Table 4 shows that quantitatively there was no retention of ketones in the system after a discontinuance of the ketogenic diet, and that there was a recurrence of attacks. When the ketogenic diet is not followed and the routine qualitative tests for ketones are negative, a recurrence of attacks may be expected.

## CONCLUSIONS

Blood chemical studies of epileptic children treated by fasting and by ketogenic diet show similar chemical changes.

In patients treated by both methods, there is a marked production of ketones as evidenced (*a*) by an increased blood acetone concentration,

(*b*) by a marked excretion of acetone bodies in the breath and (*c*) in the urine.

The alkaline reserve as measured by the carbon dioxide combining power is definitely lowered.

There is a decrease in the blood sugar concentration.

On a ketogenic diet if an excess of carbohydrates is taken by the epileptic patient, the ketosis disappears and attacks recur.

The ketosis caused by fasting and by ketogenic diet is associated with a diminution or cessation of attacks. The clinical results with epileptic children treated by diets producing a ketosis will be reported later. The production of a ketosis by diet gives the greatest promise of improvement of any method as yet devised in the treatment of epilepsy of childhood

# ANEMIA IN THE NEW-BORN *

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Severe anemia in the new-born is remarkably uncommon, a fact which has become more apparent lately, for in spite of the recent interest in the study of the blood of new-born infants, few such cases have been reported (Ecklin,[1] Donnally,[2] Susstrunk,[3] and Sanford[4]). The most frequent causes of anemia at this age are probably hemorrhage, acute infections and syphilis. The hemolytic and familial forms of icterus, while associated with an anemia secondary to the more prominent symptom of jaundice, are uncommon. The same may be said for the anemia found in congenital dropsy. During pregnancy, acute infections, chronic infections (such as syphilis and tuberculosis), cardiovascular renal disease, anemia, overwork and the taking of hemolytic drugs may affect the blood of the fetus, while repeated pregnancies and abortions may act in the same way. The offspring of such mothers are more frequently weakly, and at birth may have a blood picture at the lower limit of normal, a condition which may be called relative anemia. Again, under such conditions, the blood count is rarely normal at birth.

## REPORT OF A CASE

*History.*—L. A., a girl, white, was born, June 2, 1925. The father, aged 35, and the mother, aged 33, had always had good health. The mother had been pregnant seven times. The first four children were living and well. The fifth child died at the age of 8 days from a severe umbilical hemorrhage. The sixth pregnancy resulted in a spontaneous abortion at six weeks, and the product of the seventh pregnancy was the infant here described. The parents had been married ten years. During this pregnancy the mother's health was good, the only complaint being slight edema of the ankles. The blood pressure and urine were normal throughout the course of the pregnancy. There was no history of severe illness during pregnancy, and no drugs had been taken. The venereal history of the parents was negative.

The labor began at term and was normal in all respects. The estimated amount of blood lost during delivery was from 200 to 300 cc. The birth weight was 7 pounds (3,175 Gm.).

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* Received for publication, Sept. 24, 1926.

* From the Pediatric Department of the Salt Lake County Hospital.

1. Ecklin, T.: A Case of Anemia in the New-Born, Monatschr. f. Kinderh. **15**:425, 1919.

2. Donnally, H. H.: Anemia in New-Born, Am. J. Dis. Child. **27**:369 (April 1) 1924.

3. Susstrunk, G.: Severe Anemia in a New-Born, Ztschr. f. Kinderh. **38**: 586 (Aug.) 1924.

4. Sanford, H. N.: Anemia in a New-Born Infant, Am. J. Dis. Child. **30**: 19 (July) 1925.

*Examination.*—At birth the infant appeared to be normal and well developed and cried and breathed normally. No pallor of the skin was noted, and the tissue turgor was normal. The head was slightly molded, and there was a small caput succedaneum over the vertex. The eyes, nose, mouth and ears were normal. The heart and lungs revealed no abnormalties. The liver was normally palpable, and the spleen could not be palpated. The extremities were normal, and there was no adenopathy.

On the second day the temperature became elevated, but dropped to normal the next day. With the exception of occasional slight elevations, the temperature curve showed no abnormalities. The infant lost 9 ounces (255 Gm.) in the first two days, following which she gained normally, regaining her birth weight on the seventh day. On the twelfth day the weight was 7 pounds, 5 ounces (3,316 Gm.). Following this there was a loss of 4½ ounces (127 Gm.) which was subsequently regained, and on the twenty-first day the infant was 6½ ounces (184 Gm.) above the birth weight.

At no time was jaundice noticed. After the third day the infant became somewhat pale, and in the second week she became definitely anemic. An examination of the blood made on the thirteenth day (June 15) revealed: hemoglobin content, 31 per cent (Dare); erythrocytes, 1,200,000; leukocytes, 18,000; and a color index of 1.3—. Blood smears stained with Wright's stain showed 54 per cent polymorphonuclear neutrophils; 43 per cent small lymphocytes; 3 per cent large lymphocytes. Occasional normoblasts were seen, and there was a moderate poikilocytosis and anisocytosis. The bleeding time was four and one half minutes and the coagulation time four minutes. The blood count of the mother showed: hemoglobin, 80 per cent; erythrocytes, 4,200,000, and leukocytes, 10,200. No differential count was made. The Wassermann reaction of the blood of the mother was negative.

A physical examination on the same day showed a small, well developed infant who did not appear acutely ill. The skin was pale, free from icterus or eruption, and the tissue turgor was somewhat below normal. The head was of normal shape, and the fontanel was not tense. The conjunctivae were free from icterus, and the pupils reacted to light. Other than pallor of the mucous membranes of the mouth, the mouth, nose and ears were normal. The neck and thorax were normal, as were the lungs and heart. The liver was palpable from 1 to 2 cm. below the costal margins, and the spleen could not be palpated. The genitalia, extremities and muscles showed no abnormalities.

On the fifteenth day (June 17) the blood examination showed: 34 per cent hemoglobin (Dare), 1,280,000 erythrocytes, 14,200 leukocytes and a color index of 1.3. The differential count was: 48 per cent polymorphonuclear neutrophils, 47 per cent small lymphocytes, 4 per cent large lymphocytes and 1 per cent eosinophils. Poikilocytosis and anisocytosis were present, and normoblasts were seen occasionally.

A roentgen-ray examination of the long bones revealed no bone changes. The stools, which had been examined daily from birth, at no time gave a positive benzidin test for occult blood. The urine was normal.

The infant left the hospital on the fifteenth day in apparently good condition, except that she had marked anemia. The mother could not be prevailed on to keep the infant in the hospital any longer, as she said that all of her babies were pale at birth. She did admit that this one was much paler than any of the others had been.

On the twenty-first day (June 22) the infant was again examined. At this time she weighed 7 pounds, 6½ ounces (3,359 Gm.) and was still noticeably pale. The physical examination revealed no change from prior examinations. The spleen was not palpable. Examination of the blood showed: hemoglobin, 23 per cent (Dare); erythrocytes, 1,450,000; leukocytes, 6,000; color index, 0.8. Polymorphonuclear neutrophils numbered 49 per cent; small lymphocytes, 44 per cent; large lymphocytes, 5 per cent; eosinophils, 1 per cent, and basophils, 1 per cent. The red cells showed a few poikilocytes and no normoblasts.

The infant was then lost sight of until the age of 1 year. The history in the interval had been uneventful. The infant had gained well, and her mother stated that she had gradually lost her pallor after three or four months. Except for a moderate case of whooping-cough and a few mild "colds," she had had no illnesses. At that time the child had four teeth, crawled and was able to pull herself up on her feet.

Examination on June 5, 1926, revealed a well nourished child, with normal tissue turgor. No pallor was noticed. The weight was 22 pounds (10 Kg.) Examination revealed no abnormal condition except moderate rickets. The hemoglobin content (Dare) was 90 per cent; the erythrocyte count 4,460,000, and the leukocyte count 9,700. Blood smears prepared with Wright's stain showed the following differential count: polymorphonuclear neutrophils, 26 per cent; small lymphocytes, 49 per cent; large lymphocytes, 24 per cent; eosinophils, 1 per cent. The erythrocytes showed no abnormalities. The examination of the mother's blood showed: hemoglobin, 90 per cent; erythrocytes, 10,600. The differential count was: polymorphonuclear neutrophils, 73 per cent; small lymphocytes, 20 per cent; large lymphocytes, 4 per cent; eosinophils, 2 per cent, and basophils, 1 per cent.

## COMMENT

This case differs in some respects from the others reported. Throughout the period of observation, the infant showed no abnormalities other than pallor. It is interesting to note the absence of splenic enlargement, which condition was present in all the other cases reported. Jaundice was absent, as in the case reported by Donnally.

As far as the etiology of this case is concerned, little can be discovered. The fact that the mother had seven pregnancies in rapid succession, together with her statement that all of her infants had been pale at or shortly after birth, may have some bearing on the case; but, other than this there is no evidence to support the idea that the condition of the mother during pregnancy had anything to do with the production of the anemia in the infant. There were no manifestations of internal or external hemorrhage, nor were there any observations suggestive of excessive blood destruction. The decrease in hemoglobin found on the twenty-first day was evidently a part of the normal drop found in the early months of life. The presence in the circulation of immature cells showed active blood regeneration and ruled out aplasia of the hemopoietic system. Acute infection could be ruled out by the course of the temperature as well as the condition of the infant. The elevation of temperature on the second and third days was undoubtedly an instance of the so-called "inanition temperature," while the occasional elevations during the subsequent period of observation were probably manifestations of the thermolability of new-born infants. There were no physical characteristics suggestive of infection. Syphilis was ruled out by the negative history, negative Wassermann reaction and lack of roentgenographic evidence of changes in the long bones. Therefore, the etiology of this case must remain unexplained. The infant recovered, and at the age of 1 year is apparently normal.

SUMMARY

A case of severe anemia in a new-born infant is described, this being the fifth case so far reported. No definite cause could be found, and, as with the other cases reported, no explanation is offered. The infant, seen at the age of 1 year, showed no abnormalities, and the blood picture was normal.

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# STUDIES ON EXPERIMENTAL RICKETS

## XXVIII. DOES VITAMIN D PASS INTO THE MILK?*

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The numerous studies on the dietary properties of milk have established the fact that vitamins A, B and C, when present in the diet of the lactating female, pass readily into the milk. The frequent development of rickets in breast-fed infants and its almost universal occurrence in artificially fed infants are evidence that milk ordinarily does not contain sufficient vitamin D to afford appreciable protection against this disease. This fact has no significance in determining whether or not it is capable of passing into the milk if provided in the diet, since all ordinary foods are essentially lacking in this vitamin. Some experimental data have been published which are interpreted to mean that milk secreted when cod liver oil has been administered does not contain effective amounts of vitamin D.

Korenchevsky and Carr [1] and Korenchevsky [2] have reported studies on the influence of the mother's diet during pregnancy and lactation on the growth, general condition and the skeleton of young rats. At the time of their experiments they had not accepted as conclusive the evidence on which we [3] based our demonstration that the antirachitic potency of cod liver oil is due to the presence in it of vitamin D, a substance distinct from vitamin A.[4]

Korenchevsky and Carr employed the following as a basal diet: Purified casein 18, starch 52, fat 15, marmite 5 (later changed to dried yeast), orange juice 5 cc. and distilled water 50 cc. Various salt mixtures were added to this basal diet, depending on which element they desired

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* From the Department of Chemical Hygiene, School of Hygiene and Public Health, and the Department of Pediatrics, Johns Hopkins University.

1. Korenchevsky, V., and Carr, M.: J. Path. & Bact. **26**:389 (July) 1923.

2. Korenchevsky, V.: Medical Research Council, Special Report Series no. 71, 1922.

3. McCollum, E. V.; Simmonds, N.; Becker, J. E., and Shipley, P. G.: J. Biol. Chem. **53**:293 (Aug.) 1922.

4. Thus Korenchevsky states: "My experiments do not touch upon the question of the identity of these two factors, and for brevity of description and without prejudicing the question of identity, the principle concerned in influencing calcium metabolism and calcification of the skeleton will be called antirachitic factor and the diet deprived of that factor—A diet."

to make the limiting factor in their experiments. When the food mixture was to be rich in antirachitic factor, 12.5 Gm. of butter plus 2.5 Gm. of cod liver oil were the fats used. When the food was to be deficient in the antirachitic factor, cotton seed oil was used. The latter diet was called by them a — A diet. It will be apparent that their — A diet was deficient in vitamins A and D. In studying their data, we were not able to determine how far deprivation of vitamin A may have influenced the outcome of certain of their experiments, or may have affected adversely certain of their animals.

It is apparent, however, from their data that when mother rats are fed a diet rich in cod liver oil and calcium, the young are protected to some extent when they are later placed on a diet designed to produce rickets. The diet to which they refer as "deficient in fat-soluble factor" was also deficient in vitamin A. Lack of this factor probably aided in retarding growth in their young rats. When they speak of the effect of a diet rich in "fat-soluble factor" and calcium during pregnancy and lactation, it is not clear from their data whether or not the little rats ate of this diet during the latter part of the nursing period. As is well known, little rats supplement their milk diet with the food of the mother when they are 18 to 20 days of age. Korenchevsky and Carr's studies demonstrated that the addition of butter and cod liver oil to a diet deficient in vitamins A and D during pregnancy and lactation (apparently, from their records, allowing the young access to the mother's food as soon as they were capable of supplementing her milk supply from this source) exerted a marked beneficial effect on them. This was shown in the relative protection against rickets, and also in the increased calcium content of the bones of young rats treated in the manner described as compared with those whose mothers were fed a diet deficient in these vitamins and calcium. In most instances we were unable to determine from the description of their experiments to what extent the protection afforded the young may have been due to direct consumption of cod liver oil rather than to securing vitamins A and D through the mother's milk.

Hess and Weinstock,[5] in discussing the results of experiments on the antirachitic effect of cod liver oil fed during the period of pregnancy or lactation, state: "Our results indicate that cod liver oil, when given to the mother during pregnancy cannot be relied on to protect the offspring from rickets." In their study, women were given 16 ounces (475 cc.) or more of cod liver oil during the last two months of pregnancy.

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5. Hess, A. F., and Weinstock, M.: Rickets as Influenced by Diet of Mother During Pregnancy and Lactation, J. A. M. A. **83**:1558 (Nov. 15) 1924; Antirachitic Effect of Cod Liver Oil Fed During Period of Pregnancy and Lactation, Am. J. Dis. Child. **27**:1 (Jan.) 1924.

These authors demonstrate clearly in experiments with rats that the consumption by the mother before and during pregnancy and during lactation of a daily diet consisting of green food, bones, meat or brain, dry milk and whole grains, together with bread and potatoes occasionally, did not safeguard the young against rickets so as to prevent the disease developing when they were later fed diet 84, or a modified diet 84 of Sherman and Pappenheimer. This diet consisted of patent flour 95, calcium lactate 2.9, sodium chloride 2 and ferric citrate 0.1. The modified diet was obtained by substituting 5 per cent of dry milk for an equivalent amount of flour.

In another experiment Hess and Weinstock gave a pregnant rat five drops of cod liver oil daily during the last twelve days of pregnancy. This rat gave birth to four young. When the young were 28 days old two were placed on diet 84, and the other two on modified diet 84. They found that the four animals developed rickets in the usual degree; little or no protection had been afforded by feeding the mother cod liver oil during this period.

They also conducted four more experiments, feeding the mother rat cod liver oil during lactation, namely: 1. Five drops daily were given for seventeen days, which constitutes more than half the lactating period. 2. Since the young in experiment 1 did not develop marked rickets, the experiment was repeated and the same amount of oil was given to the mother for twenty-eight days; that is, during the entire lactation period. The young were then placed on the rickets-producing diet. Four weeks later the animals were killed. They had a moderate degree of rickets. 3. A mother rat was given 20 drops of cod liver oil daily throughout lactation. In relation to body weight, feeding a mother rat this amount is equivalent to giving a human infant 180 cc. daily. Hess and Weinstock state that moderate rickets developed under these conditions, thus indicating that the young had derived little benefit from the feeding of cod liver oil to the mother. 4. In another test the oil was fed directly to the young (eight young in the litter). Six drops daily were fed during the last fourteen days of the suckling period to four of these. The other four in the litter served as controls. Cod liver oil given in this way exerted a protective action. A mild form of rickets developed on the standard diet no. 84 after the usual test period of twenty-eight days.

Hess and Weinstock conclude from their results that cod liver oil given to the mother during pregnancy cannot be relied on to protect the offspring from rickets. They state that the active principle of the oil is not excreted in the milk in an adequate amount; rats receiving even large doses of cod liver oil were unable to afford protection to their young when the latter were placed on a rickets-producing diet. It did confer protection when fed directly to the animals.

No one would question the wisdom of the taking of cod liver oil by the expectant mother for the purpose of safeguarding her own calcium and phosphorus metabolism. It is of primary importance to determine whether taking vitamin D by the mother either during pregnancy or lactation tends greatly to safeguard the infant against the development of rickets. The chance observation that young rats from our breeding stock were rendered resistant to rickets as a result of feeding cod liver oil in the stock diet for a brief period, led us to make a more thorough investigation of the extent to which vitamin D can be transmitted to the young through the placenta or through the milk.

*Experimental Diets Employed in This Study*

| Stock Ration* | | |
|---|---|---|
| Wheat (soft) | 25.0 | |
| Maize (yellow) | 25.0 | Fresh whole milk (pasteurized) was given ad libitum daily; fresh cabbage or kale was given on Tuesdays and Thursdays |
| Rolled oats | 28.5 | |
| Flaxseed oil meal | 10.0 | |
| Calcium carbonate | 0.5 | |
| Sodium chloride | 1.0 | |

| Diet 3907 | | Diet 3955 | |
|---|---|---|---|
| Wheat (soft) | 78.0 | Wheat (soft) | 77.0 |
| Casein (purified) | 15.0 | Casein (purified) | 15.0 |
| Sodium chloride | 1.0 | Sodium chloride | 1.0 |
| Calcium carbonate | 2.0 | Calcium carbonate | 2.0 |
| Cod liver oil (Mead Johnson) | 4.0 | Butter fat | 5.0 |

| Diet 3143 | | Diet 3241 | |
|---|---|---|---|
| Wheat (soft) | 33.0 | Wheat (soft) | 34.0 |
| Maize (yellow) | 33.0 | Maize (yellow) | 33.0 |
| Wheat gluten | 15.0 | Wheat gluten | 15.0 |
| Gelatin | 15.0 | Gelatin | 15.0 |
| Sodium chloride | 1.0 | Sodium chloride | 1.0 |
| Calcium carbonate | 3.0 | Calcium carbonate | 2.0 |

* For some years this stock diet has proved satisfactory for the production of young rats to be used in all of our experimental work.

Diet 3907 contains all the essential nutrient principles. It is rich in both calcium and phosphorus, and contains somewhat more cod liver oil than can be tolerated by rats over a prolonged period. The diet was designed to furnish a liberal amount of vitamin D.

Diet 3955 is similar to diet 3907, but is much lower in its vitamin D content.

Diet 3143 has a low phosphorus and an excessive calcium content, and is low in vitamin D. It contains sufficient vitamin A to prevent ophthalmia for a considerable period. In about three weeks, this diet produces a severe grade of rickets in young rats, depending on the season of the year and the amount of light to which the animals are exposed. A detailed description of the bone lesions produced by this diet is given elsewhere.[6]

6. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **47**:507 (Aug.) 1921.

Diet 3241 has about the same phosphorus content but less calcium than diet 3143. It also produces rickets but not so severe a lesion as does diet 3143. The bone changes which it induces are described elsewhere.[7]

## DESCRIPTION OF EXPERIMENTS

The adult female rats used in these experiments had all been reared on our stock diet. Most of them had previously given birth to one litter of young. The experiments were all conducted between November 1 and March 15. The room in which the experiments were conducted was not sufficiently illuminated to interfere with the experimental production of rickets by the diets employed for that purpose.

The experiments were divided into two series, with a varying number of phases in each. It will be clear from the discussion of the different phases of the experiment how long and during what period of nursing the female rats received the different diets. The first series to be described will be called the cod liver oil series, since diet 3907 containing cod liver oil was used as the basal diet. The second series will be called the butter fat series, since diet 3955 contained butter fat. The tibiae of many of the young rats described in the following experiments presented certain deviations from the normal histologic structures, namely: in the width of the cartilage band, its arrangement, the size, number and shape of the bony trabeculae, the width of the metaphysis, the amount of calcification and other changes. We have not recorded all of these departures from the normal in this report, since the facts which we present are sufficient to show whether or not the young received protection against rickets due to the administration to the mothers of the dietary formulas described. For control animals we used young rats from our stock, and fed them diet 3241 or 3143 for the same number of days as the young from mothers on the experimental diets were fed.

## COD LIVER OIL SERIES

*Phase 1.*—Diet 3907 was fed for a month or so to the mature female rats before mating, during pregnancy and during the first ten to fourteen days of nursing. The mother and young were then transferred to our stock diet and left there until the young weighed between 40 and 50 Gm. It should be noted that the mother and young were transferred from diet 3907 before the young were old enough to eat of the cod liver oil ration. The young in this phase were exposed, therefore, to the effects of cod liver oil during prenatal life and only that part of the nursing period when they take no food other than the mother's milk.

Rat 1 weighed 208 Gm.; she had five young, the combined weight of which was 31 Gm. One of the young died. This mother had had diet 3907 for fifty

7. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: Bull. Johns Hopkins Hosp. **33**:296 (Aug.) 1922.

days before giving birth to the young. She was left on diet 3907 for thirteen days after the birth of the young. Diet 3907 was then discontinued, and the stock diet was substituted. This was fed for eleven days. During the last week or so that the young are with the mother they always supplement the mother's milk by eating of her diet. When the young averaged about 45 Gm. in weight they were given the rickets-producing diet 3241. They were fed this diet for twenty-one days. Necropsy was performed, and notes were made on their condition with respect to rickets.

In examining the bones we followed the "line test" procedure.[8] The tibiae cut as if well calcified. There was much more blood present than is seen in the severely rachitic bone. The tibiae of two of the animals had a narrow metaphysis. There were many bony trabeculae. The other two rats had tibiae which were almost normal in appearance, although the trabeculae were not so regularly arranged as in a normal bone. When the tibiae of these rats were compared with those of young stock rats which had been fed diet 3241 for the same length of time, there was no question but that the former had suffered much less from being subjected to the rickets-producing diet than had the latter. Thus partial protection must be referred to the vitamin D which the young of the experimental group had received through the mother during prenatal life and during nursing.

Two other female rats, no. 2, weighing 231 Gm., which had eight young, the combined weight of which was 41 Gm., and no. 3, weighing 217 Gm., which had eight young, the combined weight of which was 42 Gm., were subjected to the same experimental procedure. The young of these duplicated in all essential details the observations described in rat 1.

Rat 4 weight 205 Gm.; she had eight young, the combined weight of which was 40 Gm. This mother was fed the cod liver oil diet (ration 3907) for two months before the delivery of her litter. She was also kept on this diet until the young were twelve days old. Diet 3907 was then replaced by the stock diet, which was fed for thirteen days. When the young were 25 days old they were removed from the mother and fed diet 3143. This diet was fed for twenty-two days. It has been pointed out that diet 3143 produces a more severe rickets than does 3241 when fed to young rats from the stock diet.

The tibiae of these rats were much better calcified, as shown both by the resistance to cutting and by the number of calcified areas stained by silver nitrate under illumination, than in the case of young rats from the stock diet which had been given the rickets-producing diet 3143 for a similar period. There was a medium wide metaphysis with some calcified areas in it. The rats had rickets, but the condition was not so severe as it would have been if they had not received a certain amount of vitamin D through the mother.

Rat 5, which weighed 207 Gm., and which had six young, whose combined weight was 34 Gm., had the same history as rat 4. Her six young duplicated in all essential details the results obtained with the young from the latter.

Rat 6, weighing 253 Gm., which had seven young, whose combined weight was 41 Gm., had the same history as did rats 4 and 5. Her young were left on diet 3143 for forty-one days before their bones were examined. Even during this long period, diet 3143 produced only a moderate grade of rickets. In young from the stock diet we observed severe rickets under these conditions.

The outcome of these experiments makes it clear that when female rats are fed cod liver oil before mating, during pregnancy and during the first two weeks of nursing, the young are afforded an easily demonstrable amount of protection against rickets. This is shown by their ability to withstand more or less nearly completely the effects of a diet which in

8. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **51**:41 (March) 1922.

stock animals produces moderately severe rickets, and to withstand to an easily demonstrable degree the effects of a diet which produces in stock rats a severe grade of rickets.

*Phase 2.*—Diet 3907 was fed to adult female rats before mating, during pregnancy and nursing, and the young were continued on the diet until their weights averaged from 40 to 45 Gm. It will be noted that the young in this phase ate of the cod liver oil ration during the latter part of the nursing period. They were then placed on diet 3143 for fifty-six days. Eight mothers, nos. 7 to 14 inclusive, and their young were subjected to this regimen. The young did not develop rickets even though confined to this rickets-producing diet, but their bones were not of normal structure. The cartilage band was somewhat irregular; the bones were fairly well calcified. The animals were long and lithe in contrast to the stocky form of the rachitic rat.

These results confirm those of Korenchevsky and Carr, and of Hess and Weinstock, which show that feeding cod liver oil directly to the animals does confer a marked protection against rickets.

*Phase 3.*—Female rats in this phase of the experiment were fed diet 3907 for approximately one month before mating, also during pregnancy and up to the day of delivery. When the young were born, diet 3907 was replaced by the stock diet. Mother and young were fed the stock diet until the young weighed from 40 to 50 Gm. The latter were then fed diet 3143 for forty-three days.

Rat 15, weighing 239 Gm., which had eight young whose combined weight was 42 Gm., had the history just described. Two of her young, after being on diet 3143 for forty-three days, had tibiae which were in a condition suitable for making the "line test"; that is, the provisional zone of calcification was free from healing. There was a clean, wide metaphysis. The remainder of this litter had a fairly severe grade of rickets, but there was some healing along the zone of provisional calcification. This may have been a chronic state of rickets which sometimes occurs in animals fed diet 3143 for more than forty days. The litter of this female was not protected much (if any) by the taking of cod liver oil by the mother during pregnancy only. Our experimental conditions were probably too severe to reveal a slight degree of protection.

Rat 16, weighing 231 Gm., whose six young had a combined weight of 39 Gm., had the same history as rat 15. These young developed a fairly severe grade of rickets, but it was decidedly less pronounced than is regularly produced in young rats from the stock diet. Feeding cod liver oil to the mother of this litter afforded some protection.

Rat 17, weighing 270 Gm., whose seven young had a combined weight of 42 Gm., had the same history as rats 15 and 16. The tibiae of this litter were not so rachitic as were those of the other two litters. There was a mild grade of rickets present, but there was much more calcification in the bones than in the other litters with a similar history. It is not clear why this litter was more protected than were the others.

Although these three litters of young were not uniform in their response to the feeding of cod liver oil to the mother, there can be no doubt that a certain degree of protection was afforded. The mothers

did not receive cod liver oil after the beginning of milk secretion, and so whatever vitamin D they may have transmitted to their young was transferred through the placenta or through the milk from such a reserve of the vitamin as they may have been able to accumulate in their tissues. It is probably true that giving cod liver oil only during pregnancy cannot be relied on to afford much protection against rickets in the young.

*Phase 4.*—Adult female rats were fed the stock diet before mating, during pregnancy and until their young were born. *Diet 3907 (cod liver oil diet) was then substituted* for fourteen days. The mother and young were then returned to the stock diet and left there until the young weighed about 45 Gm. The young were then fed diet 3143 for thirty-five to forty-five days in different experiments. It was only during two weeks of nursing that the mother rat had access to cod liver oil.

Rat 18, weighing 200 Gm., whose eleven young had a combined weight of 58 Gm., had the dietary treatment just described. After these young had been confined to diet 3143 for forty-three days, they had fairly well developed rickets. After fifty-eight days they had well developed rickets.

Rat 19, weighing 235 Gm., whose ten young had a combined weight of 46 Gm., had a history that was the same as that just described with regard to the diet. The young were comparable to those of the preceding experiment in respect to the condition of the bones.

It is apparent from these results that the young were not protected by the mother being fed cod liver oil during the first two weeks of the nursing period only. The method of procedure was probably too severe to reveal a slight tendency to protection of the young against rickets.

Further experiments were conducted along this line. Pregnant female rats were taken from the stock diet when they were about to deliver their young. When the young were delivered, the mother was fed diet 3907 and continued on it for from fourteen to eighteen days. When the young were able to crawl about the cage, the mother and young were put back on the stock diet and left there until the young averaged 45 Gm. in weight. The latter were then fed diet 3241 for twenty-one days.

Rat 20, weighing 307 Gm., had eight young whose combined weight was 48 Gm. The mother was fed diet 3907 for seventeen days after the delivery of her young. At this time she was transferred with her young to the stock diet, on which they were kept for eleven days. The young were placed on diet 3241 and left there for twenty days. It was evident from the sections of the tibiae that the young had been protected by nursing from a mother that had taken cod liver oil only during early lactation. There was a narrow metaphysis, demonstrating that the young had developed mild rickets, but the condition was not nearly so severe as that seen in the control animals. Since this mother had access to cod liver oil during seventeen days of nursing and the young were protected in some degree from rickets, there can be no qestion that vitamin D does pass into the milk.

Rat 21, weighing 262 Gm., had eight young, whose combined weight was 52 Gm. She was treated in the same manner as rat 20. Her young were also protected to a similar degree.

Rat 22, weighing 285 Gm., which had eight young, whose combined weight was 46 Gm., had the same history as rats 20 and 21. These young were likewise protected in a similar degree.

These experiments leave no room for doubt that when the mother rat is fed a diet containing an abundance of vitamin D, her young secure this through the milk. It is apparent, however, that if the young are subjected to a severe rickets-producing diet and are left on it for from forty to fifty days, as was the case with the young of rats 18 and 19, the treatment is too stringent, and protection fails in great measure. Diet 3143 is probably a much more severe rickets-producing diet than would ever be encountered in infant feeding. However, when the mild rickets-producing diet 3241 is employed, the animals exhibit the protective influence of vitamin D.

We believe that this accounts for the results which Hess and Weinstock observed when using diet 84. This diet induces an extraordinarily severe grade of rickets, and is so defective in several respects that it debilitates the young rats in a marked degree. As a result of weakness and the severity of defects in the diet, they were unable to show the beneficial influence of securing through the mother a small or moderate amount of vitamin D.

*Phase 5.*—Adult female rats were fed diet 3907 for four to six weeks before mating, also during pregnancy and lactation. When the young were old enough to crawl about, the feeding cup was removed and the mother was fed in a separate cage. The young were limited to the mother's milk as their sole food; they had access to vitamin D in the uterus and also through the mother's milk.

Rat 23, weighing 225 Gm., had twelve young, the combined weight of which was 67 Gm. When they were 22 days old, six young were removed from the mother. The other six were left to nurse from her, receiving no food other than her milk. These six weighed 130 Gm. at this time. Ten days later they were fed diet 3143, which was continued for forty-six days. The animals remained considerably undersized. Their bones were soft and they had severe rickets. It is probable that the litter was too large for the supply of milk which the mother had to give them.

Rat 24, weighing 240 Gm., had six young, whose combined weight was 32 Gm. When they were ready to crawl about the cage the food was removed, as in the case of rat 23. When they were 26 days old they weighed 168 Gm., collectively. They were put on diet 3143 and left there for forty-five days. They developed a mild grade of rickets. This was apparently due to the fact that they had not grown sufficiently to induce a severe grade of the disease. The bones were fairly well calcified. It appears that they were protected from severe rickets by being stunted in growth.

We do not believe that we have demonstrated in these experiments that young rats are protected against rickets by the inclusion of cod liver oil in the diet of the mother during a period before mating, during pregnancy and the entire nursing period, when no food was supplied to the young other than the mother's milk. The problem is complicated by

the fact that under these circumstances the young do not secure sufficient food to enable them to develop in early life so that they have sufficient vigor to make a rapid growth possible on the rickets-producing diet. Rapid growth is essential for the development of severe rickets.

*Phase 6.*—Adult females were fed the stock diet until their young were born. On the day of birth of the young, the mother was fed diet 3907 in place of the stock diet. Mother and young were continued on diet 3907 until the young weighed about from 40 to 45 Gm.; in other words, these young had access to vitamin D from cod liver oil during nursing and also through eating of the ration.

Rat 25, weighing 256 Gm., had seven young, whose combined weight was 33 Gm. They were fed as indicated above. When the young were 27 days old they were placed on diet 3143, which was continued for forty-five days, when their tibiae were sectioned. Although they were not strictly normal, there was much protection against rickets. The animals were in good condition, that is, they did not present the appearance of the typical rachitic rat.

Rat 26, weighing 232 Gm., had eight young whose combined weight was 48 Gm. They were fed as described above. When the young were 21 days old they were given diet 3143. After forty-three days on this diet they had a mild grade of rickets. There was a narrow, irregular metaphysis. The cartilage band was rather irregular, with a few tongues of cartilage cells protruding into the metaphysis. These rats were not so much protected as the litter described above, since the former ate the ration for six days longer. The young of rat 26 were also continued on the diet 3143 twenty-four days longer. It is clear from these experiments that the young are protected by consuming vitamin D.

### BUTTER FAT SERIES

This series was planned in parallel with the cod liver oil series described in the foregoing. The diets employed were essentially alike, except that in the present series butter fat replaced cod liver oil.

*Phase 1.*—Diet 3955 was fed before mating, during pregnancy and during the first twelve to fifteen days of lactation. The mother was then fed the stock diet, and the young also ate of the diet until they weighed between 40 and 50 Gm. The young were then fed diet 3143 for varying periods before the bones were examined.

Rat 27, weighing 196 Gm., had eight young, whose combined weight was 51 Gm. This mother had been fed diet 3955 for fifty days before the young were born, and was continued on it for twelve days longer. The mother and young were then returned to the stock diet for fifteen days. The young were then placed on diet 3241 for twenty-one days, when their tibiae were sectioned.

Diet 3241, as has been stated, produces a moderately severe grade of rickets when fed for twenty-one days to young rats reared on the stock diet. The young of rat 27 developed a mild grade of rickets during the twenty-one days on diet 3241. Each tiba had a narrow metaphysis. There were many more bony trabeculae present than were found in the control bones. The little rats were protected to some extent, but not to an extent comparable to that of those whose mothers were fed cod liver oil during pregnancy and during the first twelve days of nursing. (Rats 1, 2, 3 and 4, phase 1 of the cod liver oil series.)

Rat 28, weighing 179 Gm., had eight young, whose combined weight was 43 Gm. This rat had the same history as rat 27. Only two of the litter showed

much protection. The majority of the animals were comparable to the controls with respect to the severity of rickets. Three other females, rats 29, 30 and 31, were treated in the same manner as rats 27 and 28. Their young showed some variation in the extent of the protection afforded them. At best the protection was slight, and not comparable with that observed in similar experiments in which the butter fat was replaced by cod liver oil.

Two other females had the same histories as rats 27 to 31, except that the young were confined to diet 3143, which is the more severe rickets-producing diet.

Rat 32, weighing 302 Gm., had six young, whose combined weight was 30 Gm. This rat was fed for a time previous to mating, during pregnancy and during the first seventeen days of lactation on diet 3955. At this time the stock diet was substituted for diet 3955. The mother and young were fed the stock diet for eight days. When the young were 25 days old they were put on diet 3143 for forty-one days. Three of the six rats showed no evidence of protection, whereas the other three showed a small amount of healing.

Rat 33, weighing 250 Gm., had six young, whose combined weight was 35 Gm. Her history was the same as that of rat 32. When the young were 14 days old they, with the mother, were fed the stock diet and left on it for eight days. When they were 22 days old they were fed diet 3143 and continued on it for forty-two days. These animals developed pronounced rickets comparable to the rickets which develops in animals receiving the rickets-producing diet after they have been reared on the stock diet.

It is evident from these experiments that a highly satisfactory diet without cod liver oil before mating, during pregnancy and during the first two weeks of nursing, does not appreciably protect the animals when they are later confined to a severe rickets-producing diet. It is evident, however, that when mother rats are fed as in this phase of our experiment there may be protection, provided the rickets-producing diet to which the young are later subjected is not designed to induce the most severe form of the rachitic lesion.

*Phase 2.*—Diet 3955 was fed before mating, during pregnancy and until nursing was completed. That is, the young ate of diet 3955. When they weighed about 45 Gm. they were fed diet 3143 and continued on it for about forty days.

Rat 34, weighing 285 Gm., had eight young, whose combined weight was 45 Gm. They were subjected to diet 3955 as described above. When the young were 25 days old they were fed diet 3143 and left on it for forty-three days. The tibiae were sectioned and were found to be rachitic. The metaphysis, however, was not so wide as is usually seen when stock rats are fed this diet for a comparable period.

Rat 35, weighing 197 Gm., had twelve young, whose combined weight was 62 Gm. These were treated as rat 34. When the young were 22 days old, only three were alive. When 27 days old, they were fed diet 3143 for thirty-six days. They developed severe rickets.

These experiments demonstrate that even though the mother rat was fed before mating, during pregnancy and the entire period of lactation on a highly satisfactory diet, but low in its vitamin D content, little or no protection was conferred on the young.

*Phase 3.*—The stock diet was fed to adult female rats until the young were born. From the day of delivery the mother was fed diet 3955. When the young were able to crawl about, the feeding pan was removed so that the young were confined solely to the mother's milk. The mother was fed in a separate cage.

Rat 36, weighing 154 Gm., had six young, whose combined weight was 35 Gm. When the young were 17 days old, the feeding pan was removed from the cage; when they were 31 days old, they averaged 27 Gm. in weight. They were fed diet 3143 for forty-three days; they did not grow to any appreciable extent while confined to this diet. When necropsy was performed, the stomachs were full of food, indicating that failure to grow was not due to lack of food consumption. They did not have the appearance of animals which had developed rickets. The bone section showed that they had not developed rickets or at most only of the mildest grade. There was no definite metaphysis. The bones gave one the impression that very little growth had taken place. The junctions of the ribs were thickened but they were not beaded, as are the ribs of stock animals fed diet 3143 for the same length of time. It is probably true that these little rats were not sufficiently vigorous to grow sufficiently on diet 3143 to develop rickets.

Rat 37, weighing 229 Gm., had six young, whose combined weight was 33 Gm. These animals had the same dietary treatment as rat 36. When the young were 29 days old they averaged 28 Gm. in weight; at this age they were placed on diet 3143 and left there for forty-one days. These rats also remained small. There was not a great deal of bone present in the sections; they had developed a mild grade of rickets. It was clear that they had not grown sufficiently to develop a severe grade of the disease. The possibility that the milk supply was too small forms a complicating factor in these experiments. Our test was possibly too severe to have detected a moderate degree of protection.

## COMMENT

It is clear from these two series of experiments that the diet of the pregnant and nursing mother is of paramount importance in determining the quality of milk which she will produce. We have demonstrated that when female rats are fed cod liver oil before mating, during pregnancy and during the first two weeks of nursing—that is, the little rats themselves did not eat of the cod liver oil ration—the young are afforded an easily demonstrable protection against rickets. This is shown by their ability to withstand more or less completely the effects of a diet which, when fed to little rats fed the stock diet until they weighed about 40 to 50 Gm., produces moderately severe rickets; and to withstand to an easily demonstrable degree the effects of a diet which when fed to similar stock animals produces a severe grade of rickets.

It is also demonstrated that even though the mother and young take a diet which induces excellent growth, fertility and the rearing of a large majority of the young, that is, one containing satisfactory protein, mineral content, vitamins A and B and a small amount of vitamin D, it does not necessarily induce sufficient vigor in little rats to enable them to withstand the effects of a severe rickets-producing diet. This confirms the observations of Hess and Weinstock, but offers a somewhat

different interpretation of the observed facts. Our data show, however, that when the mother rats are fed a highly satisfactory diet before mating, during pregnancy and during nursing, but when the young are not allowed to eat of the ration containing butter fat (see phase 1 of the butter fat series) some protection is afforded which can be demonstrated if the rickets-producing diet to which they are later subjected does not induce too severe a form of the disease.

Results such as the foregoing point to the need for a better appreciation of the significance to the child of being endowed with a superior physical inheritance. Several cases have been recorded in which infants have had rickets at birth or within the first weeks of postnatal life. Experiments with young rats illustrate how in this species the dietetic management of the mother during pregnancy may predispose the young to rickets or render them more or less refractory to the disease. Provision of a diet which is so constituted as to insure good quality of the mother's milk—including a considerable amount of the antirachitic vitamin D—will tend markedly to safeguard the vitality and development of the young during the early weeks of life. The prevalence of rickets among both breast-fed and bottle-fed infants may in part be due to the unsatisfactory condition of the expectant and nursing mother brought about by an unwise selection of food. Even a diet which is well constituted except for a deficiency of the antirachitic vitamin may, in the absence of an appropriate amount of sunlight, fail to safeguard the young against malnutrition resulting in rickets, especially when the food of the young is deficient in vitamin D as it becomes independent of the mother. It seems justifiable, therefore, to insist on the importance of the expectant mother and the nursing mother taking suitable amounts of cod liver oil, as well as the importance of giving it to the infant.

The studies reported in this paper also suggest the probable reason why certain physicians have observed that cod liver oil fails to protect against rickets in some infants. Animal experiments make it clear that faulty nutrition during prenatal life and the early part of the nursing period may so debilitate the young that later a dietary regimen which one would expect to protect against rickets may fail to do so. It cannot be too strongly emphasized that a highly satisfactory diet, that is, one containing milk, fresh fruits, leafy vegetables, moderate amounts of meat and eggs, and less of the highly refined foods such as flour, cornmeal, polished rice, sugar and foods made from these, is of paramount importance for promoting the welfare of both mother and young. Such a regimen is little less important at other periods in life if one would realize the optimum of health. It is not to be expected that a pale, anemic, frail woman, whose vitality has been undermined by faulty living, should be successful in trying to build herself up by a dietary reform early in pregnancy. It is much easier to maintain than to regain health.

SUMMARY

It is clear from these experiments that when female rats are fed cod liver oil before mating, during pregnancy and during the first two weeks of nursing, their young are protected to a certain degree against rickets when they are later subjected to a rickets-producing diet.

Our experiments demonstrate that the vitamin D of cod liver oil does pass into the mother's milk.

A satisfactory diet, except that it is low in its vitamin D content, when fed to female rats before mating, during pregnancy and during lactation, does not necessarily confer much protection on their young when the young are later fed a rickets-producing diet.

A possible explanation for the results secured by Hess and Weinstock, which they interpreted as indicating that the young were not protected when the mother was fed cod liver oil during pregnancy and nursing, is offered.

An explanation is suggested for the high incidence of rickets among children, and for the occasional observation that the administration of cod liver oil fails to protect infants against this disease.

# PURPURA FULMINANS DUE TO THE MENINGOCOCCUS

## REPORT OF A CASE *

SINCLAIR BATTLEY, M.B. (Toronto)

DETROIT

A case of purpura fulminans is reported which is of interest because of its comparative rarity, the etiology of meningococcus infection and the opportunity for complete necropsy studies.

### CASE REPORT

*History.*—A boy, aged 10 months, had previously been a normal healthy child. On the morning of the day before death his mother brought him to the outpatient clinic, at which time he appeared to be well. He was vaccinated for smallpox. The same afternoon at about 5, it was noticed that he was not well; he had fever and chills and was restless. The manifestations of illness increased during the evening. By 10 p. m. he presented the appearance of an acutely ill, pale and slightly cyanosed child, with a temperature of 104 F. and a respiratory rate of 52. Physical examination gave negative results, except for a general hyperesthesia and distress elicited on moving the joints. The impression at the time was that of a child in an early stage of pneumonia. Early the following morning, bluish red blotches appeared in the skin at various points, particularly on the face and buttocks. Some of these increased rapidly in size, the larger being 3 or 4 cm. in diameter, while most were from 0.5 to 1 cm. These markings, obviously hemorrhages, were also present in the palpebral conjunctivae and in the mucous membranes of the mouth. Physical examination revealed nothing additional except purpuric spots and a slight bulging of the fontanel which was not sufficient to be of diagnostic value and was unaccompanied by other neurologic signs.

The infant was admitted to the inpatient department of the hospital, and shortly after admission a change was noticed; the breathing became irregular, the extremities cold, the body cyanotic and the baby appeared to be sinking into a state of collapse. On puncturing the finger to determine the bleeding time, it was found that the blood did not flow. It seemed as if circulation in the extremities had ceased already, although the heart was beating strongly. Nystagmus appeared shortly after this, convulsions occurred and death ensued almost immediately. The total duration of the illness was twenty hours.

Studies of the blood disclosed: red blood cells, 3,430,000; white blood cells 13,400; polymorphonuclears, 47; polymorphonuclear eosinophils, 2; small mononuclears, 22; large mononuclears, 22; transitionals, 5; platelets, 216,000. The coagulation time of the blood by the Howell tube method was normal.

Urinalysis (obtained postmortem) was negative except for albumin, 2+. A blood culture taken eighteen hours after the onset of illness showed a growth of meningococcus after several days, and agglutination with therapeutic polyvalent serum was complete in a dilution of 160.

*Necropsy.*—The points in the necropsy bearing on the present condition were as follows:

Several small hemorrhages were present in the pleura and on the epicardium around the distribution of the coronary artery. Numerous tiny hemorrhages were present in the capsule of the thymus gland. The suprarenals were purplish with

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* From the Department of Pediatrics of the Henry Ford Hospital.

mottlings of darker purple. On section, the cortex and medulla both had a reddish purple color, and the normal structure could not be identified because of the presence of much blood.

The meninges presented no abnormal characteristics. The blood vessels on the surface of the brain were much distended. The subarachnoid spaces contained a great deal of almost clear watery fluid, and the cisterna cerebellomedullaris was much larger than normal. Spinal fluid was obtained by puncture into the cisterna before the cranium was opened, and 30 cc. of fluid was obtained. Both middle ears were punctured and were normal. After hardening the brain in liquor formaldehydi, sections through it showed no abnormalities except that the small vessels were distended with blood. The spinal fluid obtained showed 60 cells per cubic millimeter. No intracellular or extracellular organisms were found, and cultures showed no growth after seven days.

*Microscopic Observations.*—There was extensive obliteration of the normal structure of the suprarenals by massive hemorrhage, which was most marked in the medulla. Sections of the skin taken through a purpuric area showed great dilatation of the blood vessels of the corium. There was surrounding hemorrhage into the fibrous tissue and about the blood vessels in the adipose tissue. The epidermis was normal, and there were no vesicles. The brain showed no abnormality except some thickening of the leptomeninges and a slight dilatation of the blood vessels of the cortex. Bacterial stains, according to MacCallum's method, were made of the sections of various tissues, and in the skin and uvula gram-negative organisms having the morphology of the meningococcus were found. In the skin and in blood vessel lumina these were intracellular; in the uvula, they were both intracellular and extracellular within a moderate sized blood vessel.

## COMMENT

The usual classification of purpura is into primary purpura, that type having as its basis a marked diminution of the blood platelets, and secondary, or symptomatic, purpura. The symptomatic purpura is subdivided into four types: first, mechanical purpura such as sometimes occurs after severe paroxysms of coughing in pertussis; second, toxic, such as is occasionally seen in poisoning by metals or drugs; third, cachectic, which appears during the course of wasting diseases or in the aged; fourth, infectious purpura, found in various infections, of which the case reported is an example.

Hemorrhagic spots in the skin have been observed in a great many infections. In some instances they form a regular feature of the disease in all or in a large proportion of cases, as in typhus fever, in the rose spots of typhoid or in meningococcic infections in which their presence has given rise to the name "spotted fever." Purpura in cerebrospinal meningitis occurs in a varying number of cases up to 25 per cent, usually appearing on the third day of the disease and consisting of a fine petechial rash. It seems true that in epidemics such as were seen in army camps, the incidence of purpuric manifestations is increased. In the hyperacute or fulminant type frequently seen in children, large purpuric spots are invariably a marked feature. In these the rash appears shortly after the patient becomes ill, and death occurs very soon. Purpura is of less frequent occurrence in other infections, such as in the hemorrhagic type of smallpox, measles, scarlet fever and diphtheria, and in these is evidence

of a severe type of disease. Often, fatal purpuric attacks have occurred during the convalescent stage of various infectious diseases, and in conditions without demonstrable etiology attacks with a fatal outcome have been described. In obscure infections, the fact that blood cultures were not often obtained and that the meningococcus is difficult to grow, leads one to suspect that the same agent may have been at work in many similar conditions.

Donald [1] reported a case occurring during the convalescent stage of dysentery in which the patient died in seven days. The etiology was not determined, but it is possible that this may have been a meningococcic sepsis occurring because of the patient's weakened condition. Lommen [2] cited a case almost similar to ours, in which no definite cause was found. Bischoff [3] reported a similar case, with acute fulminating toxemia, in which no etiologic factor was determined. Dwyer [4] reported a case of acute hemorrhagic purpura in which death occurred in one day, and in which he suspected the meningococcus as being the causative factor. In a case reported by König [5] a positive streptococcic blood culture was obtained. In fatal pneumococcus infections in children, Nobécourt and Mathieu [6] have noted the occurrence of purpuric eruptions. A case of purpura fulminans during convalescence from scarlet fever was recorded by McConnell and Weaver.[7] A child, aged 6 years, showed large patches of purpura several inches in diameter covering large portions of an arm and a foot, and death soon occurred. Kelly [8] reported purpura fulminans following measles, with death ensuing in fourteen hours. That a picture identical with that of the purpura of meningococcus sepsis can occur with other blood infections is shown by the report of Brunsgaard and Thyøtta.[9] They report a case of gonococcic sepsis in an adult, in whom the organism was obtained from the blood and meninges and from the patches of fresh purpura. The case of Weil

1. Donald, W. M.: A Case of Purpura Fulminans, Arch. Pediat. **33**:844 (Nov.) 1916.

2. Lommen, P. A.,: Case of Purpura Fulminans, J. A. M. A. **75**:1569 (Dec. 4) 1920.

3. Bischoff, H.: Zur Frage der Purpura Fulminans, Monatschr. f. Kinderh. **28**:481 (Sept.) 1924.

4. Dwyer, H. L.: Purpura Fulminans, J. A. M. A. **78**:1187 (April 22) 1922.

5. König: Purpura Fulminans bei einem 19 monatigen Kinde, Ztschr. f. Kinder. **32**:282 (May) 1922.

6. Nobécourt, P., and Mathieu, R.: Le purpura dans les pneumococcies des nourrissons, Arch. de méd. d. enf. **23**:689 (Dec.) 1920.

7. McConnell, G., and Weaver, H. L.: Purpura Fulminans During Convalescence From Scarlet Fever, J. A. M. A. **78**:165 (Jan. 21) 1922.

8. Kelly, E. H.: Case of Purpura Fulminans Following Measles, Brit. J. Child. Dis. **19**:86 (April-June) 1924, abstr. Proc. Roy Soc. Med. **15**:45 (Aug.) 1921.

9. Brunsgaard, E., and Thyøtta, T. L.: Gonokokmeningit med gonokok-purpura, Norsk. Mag. f. Lægevidensk. **85**:809 (Oct.) 1924.

and Azoulay,[10] also occurring in an adult, showed that the same condition occurred with the staphylococcus. In this case, one of staphylococcic septicemia arising from a prostatic abscess, purpura resembling the meningococcus type was present.

Elliott and Kaye [11] reported a meningococcus infection occurring in two soldiers in the British army; one died in twenty-four hours, while the other recovered after a severe illness, during which suppuration occurred in the purpuric areas, and amputation of both feet became necessary. They emphasize the point that although no signs of meningitis are present, this type of rash is always suggestive of meningococcal infection. Le Bourdellès [12] reported twenty-six cases of purpura, one being of a fulminating type, in twenty-two of which the meningococcus was recovered. In seventeen of these cases positive blood cultures were obtained, and in eight no meningeal involvement occurred. Of the remaining four cases, three were diagnosed as meningococcic on strong presumptive evidence, and one as being due to *Micrococcus melitensis*. Herrick [13] feels that the meningococcus is the almost universal cause of fulminating purpura, and gives in support of this view his experience in army camps in which the disease was not rare. He says:

> In the vast amount of acute infectious disease studied among recruits, cases showing tonsillitis, pain in the bones and joints, arthritis, vomiting, rapid pulse, low blood pressure, marked leukocytosis and rapidly developing purpura were uniformly, in the experience of military surgeons, examples of meningococcus sepsis. Purpura in measles, scarlet fever, pneumonia, influenza, and other infectious diseases among the troops was extremely rare, and when it occurred was never the widespread, rapidly developing form described by Dr. Lommen and which to the practiced army surgeon meant just one type of infection. It is important to recognize the fact that many of these cases of meningococcus sepsis do not develop meningitis. It is also important to emphasize the brilliant results following massive intravenous serum therapy in just this type of case.

In the epidemic of cerebrospinal meningitis of 1866 in Ireland, the eruption was so frequent and so severe that the disease became known as the "black death," a term used in the Middle Ages to signify plague.[14] In the fulminant type the organisms may never reach the meninges, but the patient succumbs while still in the septicemic stage. The most striking features are either wild delirium or profuse coma, marked cyanosis and many definite purpuric spots. Ker [15] gives as his case with the

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10. Weil, M. P., and Azoulay, R.: Purpura aigue staphylococcique, Bull. et mém. Soc. méd. d. hôp. d. Paris **48**:258 (Feb. 29) 1924.
11. Elliott, T. R., and Kaye, H. W.: A Note on Purpura in Meningococcal Infections, Quart. J. Med. **10**:361 (July) 1917.
12. Le Bourdellès, B.: De la frequence de la meningococcie, une forme pupurique, Presse méd. **33**:660 (May 20) 1925.
13. Herrick, W. W.: Case of Purpura Fulminans, J. A. M. A. **76**:55 (Jan. 1) 1921.
14. Netter, A., and Salanier, M.: The Presence of Meningococci in the Purpuric Elements of Meningococcal Infection, Brit. J. Child. Dis. **14**:101 (April-June) 1917.
15. Ker, C. B.: Infectious Diseases, The Oxford Press, 1920, p. 559.

shortest duration one lasting for twelve hours from start to finish, but states that cases have been reported in which death occurred within five hours of the onset.

It has been debated whether the cutaneous hemorrhages are the result of toxic injury to the vessels or of metastatic foci of bacterial growth. Netter and his co-workers [14] have shown that meningococci can be found in vesicles forming over the areas of purpura by examining the exudate in direct smear. This may be used as a means of diagnosis long before the organisms can be found in blood cultures, thus enabling specific treatment to be started. Indeed in some cases the organisms were found in this way when negative blood cultures were obtained. Other workers have previously shown by histologic studies that the meningococcus is present in tissue surrounding arterioles. In other reports Netter and his co-workers [16] have shown that the organisms may be demonstrated in serum obtained by scarification of the purpuric lesions.

The present case illustrates the frequent finding of hemorrhage into the suprarenal glands in rapidly fatal cases, which, according to some authors, is probably the cause of death. It also illustrates the presence of meningococcic septicemia without the development of meningitis, and presents what is probably a picture of an early stage in the localization of the infection in the central nervous system, as the increased volume of cerebrospinal fluid and increased cell count probably indicate that meningitis would have developed had the patient lived longer.

## CONCLUSION

1. A case of purpuric meningococcic sepsis with rapidly fatal outcome is reported, with necropsy studies.

2. A brief review of the recent literature is made, which gives one the impression that while purpura may be a symptom in acute types of most infections, it is most frequently found in acute and fulminating types of meningococcus infection.

3. Early recognition of the disease is necessary for successful therapy.

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16. Netter, A.; Salanier, M., and Wolfrom: A New Case of Hyperacute Purpura Without Cerebrospinal Meningitis; Recognition of its Meningococcal Nature During Life by Microscopical Examination, Brit. J. Child. Dis. **14**:104 (April-June) 1917. Netter, A.; Salanier, M., and Blanchier: Two Fresh Cases of Meningococcal Infection with the Presence of the Meningococcus in the Purpuric Eruption, Brit. J. Child. Dis. **14**:264 (Oct.-Dec.) 1917.

# CONGENITAL LYMPHANGIECTATIC EDEMA

## REPORT OF A CASE WITH NECROPSY *

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Last year [1] we reported a rare case of congenital edema which presented unusual features with reference to the lymphatic system. In this report we mentioned certain characteristics which clearly defined this type of edema as an entity different in many respects from congenital elephantiasis, further emphasized by a review of the literature.

A few months after publication of this report, the child developed an acute infection which in a short time terminated fatally. Necropsy was performed, which brought to light some unusual and interesting pathologic conditions. However, before describing in detail the necropsy observations, we shall present a brief résumé of the clinical features as embodied in our previous article.

### CASE REPORT

*History.*—H. B., a white girl, born June 10, 1923, presented the following picture: (1) a markedly edematous left foot, leg and thigh; (2) edema of the left labium majus and the right shoulder, arm, hand and fingers; (3) a complete macroglossia with edema of the right lower lip, with a sharp line of demarcation at the center, and (4) edema of the right ear, the right upper and lower lids and enlargement of the right axillary lymph nodes. The general appearance was one of gigantism or elephantiasis. The affected areas were of firm consistency with slight pitting, and the right hand presented an extreme degree of puffiness, with a sharp crease marking the wrist line. The tongue practically filled the mouth. The left side of the face, the left shoulder, arm, hand and fingers were normal in appearance.

The family history was negative. As the child grew older, little or no change was noted. The treatment included massage, elastic bandages, radium, roentgen ray and deep therapy, the administration of theobromin sodiosalicylate and thyroid extract (in increasing doses), none of which produced any effect. Examination of the blood and urinalyses were negative. At the time of death the child was 2 years old. During the later stages of her final illness, emaciation was present to a marked degree.

*Necropsy* (Performed by Dr. B. S. Kline).—The body was that of a considerably emaciated, white girl, aged 2 years. Rigor mortis was present only in the lower extremities and only in slight degree. There was slight hypostasis. The skin varied greatly in different portions of the body, and was especially altered in the right upper extremity and the left lower extremity. Here, although the skin hung in folds, there was still present apparently a moderate degree of brawny edema. The left labium was involved, together with the left lower extremity.

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1. Ruh, Harold O., and Dembo, Leon H.: Congenital Lymphangiectatic Edema, J. A. M. A. **84**:1410 (May 9) 1925.

The right side of the face was involved slightly, most prominently in the lips where the swelling stopped almost in the midline. The skin of the right hand and forearm showed considerable diffuse brown pigmentation with a few unpigmented areas in the skin of a few fingers. In all of these areas the atrophy of the soft tissues was less marked than elsewhere, where the skin was thin, wrinkled and the soft tissues apparently closed. The face was triangular in outline with the base above. There were no appreciable deformities of the eyes and nose, and little swelling of the right eye. The tip of the tongue reached to the lips; it was definitely swollen to a few times its normal size. The neck presented no abnormalities. The chest showed a good anteroposterior diameter; the costal angle was much wider than the average. There was a fulness of the abdomen

Fig. 1.—Appearance at the age of 16 months; macroglossia; edema of upper and lower right eyelids; edema of right side of lower lip.

especially in the umbilical portion. The external genitalia and extremities showed no abnormalities other than those noted in the foregoing.

On making the skin incision, little subcutaneous fat was encountered, and the muscles were small and pale. When the abdomen was opened, the viscera were seen to be normally disposed. The intestines were slightly distended throughout. In the cavity there was about 30 cc. of turbid, yellow fluid, a smear of this showing numerous large, mononuclear cells, apparently peritoneal cells, a few wandering cells and a few fat globules. The mesentery was strikingly swollen. The diaphragm reached to the fourth rib on the right side and to the fifth rib on the left side.

On opening the thorax, a striking picture was presented. The pericardial cavity, greatly enlarged, contained 85 cc. of clear, yellow fluid, a smear from which showed a few mononuclear cells. There were no abnormalities of the right pleural cavity. The left pleural cavity contained about 50 cc. of a fluid the color of coffee grounds, the smear from which revealed numerous red blood cells,

fairly numerous pus cells, wandering cells and numerous bacteria. The benzidine reaction for blood was markedly positive. The thymus was not enlarged.

The heart was not appreciably enlarged. There was less fat in the grooves than normal, which was watery in appearance. There was slight thickening of the epicardium, more marked on the right than on the left side. There were no abnormalities of the mural or valvular endocardium or the coronary vessels. The myocardium had about the average thickness, and on section appeared watery and reddish-brown.

All the lobes of the right lung were voluminous, crepitant and soggy. The elasticity appeared somewhat diminished. The pleura was not appreciably thickened, but showed prominent lymphatic channels, especially striking on the under

Fig. 2.—Edema of left leg, and of right arm and hand.

surface of the lower lobe. The glands at the hilum were moderately enlarged, firm and whitish. The pulmonary vein was somewhat dilated, and the walls appeared thickened. The pulmonary artery showed no abnormalities. On section, a moist, pink-red surface was seen. There was apparently a moderate to considerable amount of thin fluid in the air sacs, and a moderate amount of mucous in the bronchial branches.

The left lung was less voluminous than the right. Here the pleura was laterally distended to a considerable degree by clear fluid. The glands on this side were appreciably enlarged and normal in color. The pulmonary vein on this side showed no abnormalities.

The liver and gallbladder presented no abnormalities. The spleen showed no appreciable abnormalities except that the malpighian bodies were less prominent

than usual. The pancreas showed a slight increase in consistency. The suprarenals showed no abnormalities. There was abundant medullary tissue present. The kidneys were slightly enlarged. The capsule was thin and stripped readily. The surfaces were paler than normal; the lobulations were not unduly prominent. On section, the cortex was seen to be much wider than normal, paler and somewhat watery in appearance. The pelvis on each side and the ureters showed no appreciable abnormalities. The bladder was moderately distended with clear urine, and the internal genitalia showed no abnormalities.

The aorta and larger branches, the inferior and superior vena cava and larger branches showed no abnormalities. About the larger veins of the neck on the right side there was considerable thickening of the sheath and at the root of the neck. There were several enlarged, firm, whitish lymph glands adjacent to this thickened sheath. This was in decided contrast to the conditions on the opposite side of the neck, where there were no appreciable abnormalities of the sheath, and the lymph glands were but slightly more prominent than the average.

Fig. 3.—Ramifying connective tissue with dilated lymphatic channels of the tongue.

Adherent to the sheath of the external iliac vein on the left side near Poupart's ligament, there was a greatly enlarged lymph gland, firm, whitish and apparently somewhat edematous.

The tonsils, each about 7 mm. in diameter, were firm, whitish and less pulpy than the average. The thyroid was of normal size and consistency. On section no abnormalities were noted. The estimated weight of the thymus was from 6 to 7 Gm.; it was somewhat smaller and less pulpy than the average, and apparently somewhat involuted.

The esophagus showed no appreciable abnormalities, except that in the lower portion there was apparently some autolytic change in the mucosa. The stomach, of average size, contained a moderate amount of tenacious mucus. The intestines throughout were slightly distended by fluid and semisolid contents, the latter of lighter color than the average, and in the rectum of a pasty almost clay-colored appearance. There was moderate edema of the walls throughout, and the lymphatic glands appeared more prominent than the average. This was especially striking in the serosa, most markedly of the jejunum in which there were tiny sacs filled

with lymph, hanging by narrow pedicles. There was slight congestion of the mucosa in the jejunum and upper ileum. The appendix showed no appreciable abnormalities.

The mesenteric lymph glands were found considerably enlarged, firm, translucent to whitish, embedded in a strikingly edematous mesentery (mesentery, 3.5 to 4.5 cm. in width). The fat, however, greatly diminished in amount, appeared watery. The blood and lymph vessels in the mesentery were much more prominent than the average. Lymph glands of similar nature, but less markedly involved, apparently, were observed, as noted in the foregoing, adherent to the left external iliac vein, at the hilum of the right lung and at the root of the neck on the right side (in the areas related to the edematous tissues).

There were no appreciable abnormalities in the brain, except a considerable increase in the thin fluid below the pia, especially striking over the convexities toward the longitudinal sinus and near the foramen magnum. The weight was normal, and the ventricles were not dilated.

Fig. 4.—Lymph node (stage 1). Beginning dilatation and replacement of lymphoid tissue.

The thoracic duct, dissected out, showed no appreciable abnormalities except that there was a well-defined receptaculum below and above. It had two openings into the vein. The right axillary glands were palpable and moderately enlarged.

*Microscopic Description.*—Section of the myocardium showed the muscle cells in general to be about the average size. In places, however, especially near the endocardium, they were swollen. The cytoplasm was more vesicular than normal. With high power magnification, a moderate number of cells were observed in which the striations were almost completely obliterated, and the cytoplasm was stained a deep pink. The muscle bundles were separated from each other more than normally by amorphous, pink-stained material. A number of these areas suggested dilated lymphatic glands. The blood vessels were medium sized, and there was considerable dilation of the lymphatic vessels by amorphous, pink-stained material.

Section of the lung showed engorgement of the blood vessels. Many of the alveoli contained abundant amorphous, pink-stained material. The pleura and septums showed a striking picture; there was a marked increase in the areolar connective tissue, with numerous moderately engorged lymphatic vessels associated.

In a few places in the areolar connective tissue there were small mononuclear round cells. The lymphatic vessels contained few nucleated cells.

The lobulation of the liver was regular. The liver cells were of average size and showed no appreciable abnormalities. The peripheral structures showed no abnormalities.

Section of the spleen showed patchy thickening of the capsule by loose connective tissue, in which there were a moderate number of dilated lymphatic vessels. These structures had no contents within them. The venules almost everywhere showed moderate thickening of the walls. There was some engorgement with blood. The malpighian bodies were much less prominent than the average, but the lymphatic channels within them were dilated. The walls were somewhat thickened, and the contents in general consisted of an amorphous, pink-stained material. The lymphocytes were greatly diminished in number. The trabeculae and vessels showed no abnormalities.

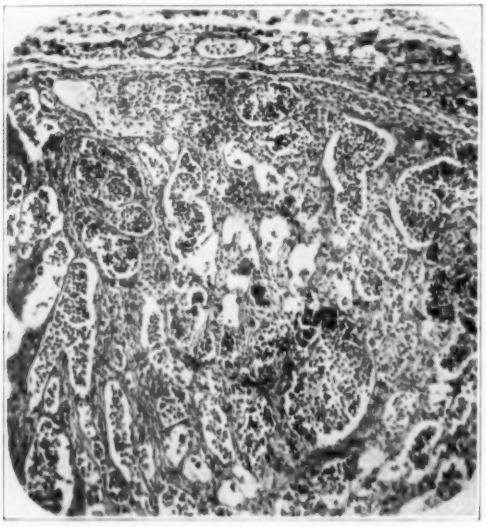

Fig. 5.—Lymph node (stage 2). Moderately advanced dilatation of lymph channels.

The islands and acini of the pancreas showed no abnormalities. The interlobular, and in places the intralobular, septums, however, showed a striking picture with numerous greatly distended lymphatic channels. These structures were apparently increased considerably in number almost everywhere. About the pancreas the mesentery or capsule showed a striking picture. This structure, about 1.5 mm. in width, was composed of almost adjoining, dilated lymphatic vessels, surrounded by a small to moderate amount of loose areolar connective tissue. In places within the connective tissue there were a few mononuclear, wandering cells. In places the lymphatic channels were apparently replacing the adipose tissue. At other places there was a moderate edema of the adipose tissue, with amorphous, pink-stained material within and between fat cells.

The cortex and medulla of the suprarenal were normal in appearance. The capsule, however, was moderately thickened, and showed numerous dilated lymphatic vessels in places.

Practically all tubular lumina and glomerular sacs of the kidneys contained amorphous pink-stained material. There were no abnormalities of the tubular epithelium or blood vessels. There was a dilated lymphatic vessel, but no contents within it.

The lobulation of the thyroid was fairly regular; the lobules were large. The acini varied in size and contained less colloid than the average. They were lined by low columnar epithelium. The majority of acini were large, and round to oval in outline. There were, however, groups of small, apparently newly-formed, acini. There were a few large lymphatic vessels in the capsule.

Section of the tonsils showed slight to moderate scarring of the lymphoid tissue. The lymphatic channels in the follicles and elsewhere were more prominent than normal, and the walls appeared thickened. The channels contained, in addition to lymphocytes, fairly numerous pus cells.

Section of the tongue showed ramifying (especially through the muscle), loose, areolar connective tissue with numerous lymphatic channels within it. In places there was slight round cell infiltration. There was also abundant fluid in this tissue (amorphous pink-stained, granular material). In general, the lymphatic channels were not dilated except just below the surface epithelium for a distance

Fig. 6.—Stage 3, lymph node (advanced). Marked replacement of lymphoid tissue by connective tissue, with dilated channels.

of about 1 mm. In a few places, however, there was considerable distention of the lymphatic vessels, with pictures suggesting rupture of the walls.

Section of the duodenum in the region of the pancreas showed numerous dilated lymphatic channels in the submucosa, with abundant amorphous pink-stained material distending this coat. There were a few dilated lymphatic vessels in the muscle. There were numerous dilated lymphatic channels in the serosa, with distention of this coat by amorphous pink-stained material. Between the serosa and the pancreas there was an area composed of adjoining lymph channels resembling a lymphangioma.

Section of the ileum showed moderate infiltration of the stroma of the mucosa by wandering cells. The lymphatic glands in all coats were strikingly prominent and everywhere dilated. In the mucosa, especially, they contained a moderate number of pus cells, and appeared greatly increased in number. This was especially striking in the submucosa which, almost everywhere, had the appearance of a lymphangioma. The muscles showed relatively few lymphatic vessels. The serosa, however, varied in width to 500 microns, composed in great part of dilated

lymph channels. Adherent to the surface in places there were distended, thin-walled lymphatic channels.

A greatly enlarged lymph gland from the region of the left iliac vein was replaced almost entirely by lymph channels, surrounded by a moderate to a considerable amount of smooth muscle, and loose, areolar connective tissue. There were, however, about ten small accumulations of small lymphocytes toward the center of the gland. The structure strikingly resembled a lymphangioma. The channels contained amorphous, pink-stained material in places; in others there were no contents.

One section of the mesenteric lymph glands showed two glands, 1 cm. in diameter, about 0.5 to 0.7 cm. in width, almost completely replaced by channels as in the gland described above. In one there was a moderate overgrowth of connective tissue, in the other, only a slight overgrowth. In the latter there was a marked distention of lymph channels by mononuclear and polymorphonuclear wandering cells, and in many places pus cells predominated. The dilatation

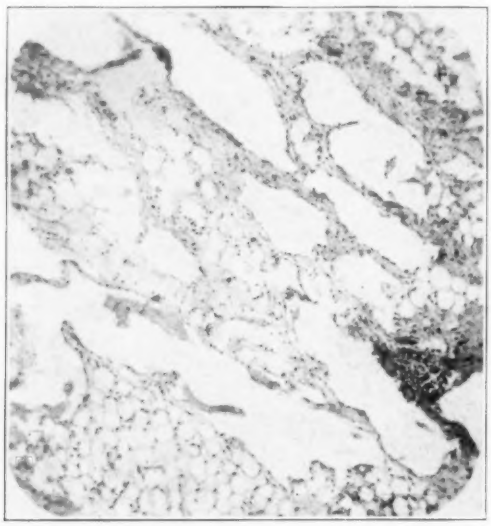

Fig. 7.—Stage 1). Mesentery; dilated lymph channels.

of the lymphatic vessels was strikingly shown in one follicle. This structure was almost completely replaced by adjoining lymph channels over 100 microns in width, and filled by wandering cells as described in the foregoing. This gland showed moderate scarring and round cell infiltration of the capsule and regional fatty tissue. The adjacent gland showed fewer wandering cells in the lymphatic channels. In both glands the atrophy of lymphoid tissue was striking. The mesentery about the glands showed moderate distention of the fibrofatty tissue by amorphous pink-stained material. There were areas of scarring and round cell infiltration. There was a moderate number of dilated lymphatic vessels present.

Five sections of mesentery showed a striking picture in all portions. Ramifying everywhere throughout the fibrofatty tissue were numerous dilated lymphatic channels, in places over 1 mm. in diameter. Some of these structures were thin-walled, while others were surrounded by a moderate to a considerable amount of smooth muscle and areolar connective tissue. Most of the latter areas were associated with lymph nodes and lymph glands which showed atrophy of lymphoid tissues and replacement by lymphangiomatous tissue. In some places the channels contained a moderate number of wandering cells, including polymorphonuclears.

In one place there was a small lymph gland showing marked overgrowth of smooth muscle and areolar connective tissue of the capsule and trabeculae, with replacement of all but the central portion of lymphoid tissue. The subcapsular lymphatic vessels were replaced by scar tissue in places; in others, they were greatly distended by an amorphous pink-stained substance and moderate number of wandering cells. In addition to the distention of the tissues by dilated lymphatic vessels, the fat in many places within and about the cells showed amorphous, pink-stained material resembling the lymph in some of the adjacent channels. In places the mesentery showed scarring and mononuclear round cell infiltration. In some places there were markedly dilated, thin-walled channels with rupture of the walls. The regional fatty tissue for a distance of 1 mm. or more showed infiltration by this pink-stained substance. Some of the dilated channels contained abundant blood. A few veins, from 1 to 2 mm. in diameter, showed strikingly dilated lymphatic glands in the adventitia. About one of the veins there was abundant amorphous, pink-stained material suggesting lymph from ruptured

Fig. 8.—(Stage 2). Moderately advanced; mesentery: dilated lymph channels and connective tissue overgrowth. Amorphous material shown in dilated lymphatic channels.

lymphatics. This fluid in places extended for a distance of 1.5 mm. about the vessel. The sheaths of the majority of small nerves showed considerable distention by amorphous, pink-stained material.

Section of the cervical gland (right side) showed replacement of lymphoid tissue by lymphangiomatous tissue as described above. A few small collections of lymphocytes were present in the center. The lymphatic vessels contained amorphous, pink-stained material. There were no wandering cells.

Section of the bronchial lymph gland (right side) showed considerable distention of the lymphatic channels, with slight to moderate thickening of the walls. There were moderate numbers of small and large mononuclear wandering cells and a few pus cells. In places the capsule was considerably thickened, as were also the regional trabeculae. In the fibrofatty tissue about the capsule, there were numerous dilated lymphatic channels filled with mononuclear and polymorphonuclear wandering cells; also a moderate number of red cells. There was also some scarring and round cell infiltration of the fibrofatty tissue about the lymph gland.

Section of the thoracic duct taken at various levels showed no appreciable abnormalities, except moderate thickening of all coats. Near the entrance into the vein, however, a few sections showed moderate scarring and round cell infiltration of the inner coats. Just beyond this point the duct showed considerably thickened inner walls. In the lumen there was a blood clot with the architecture of an antemortem thrombus.

*Anatomic Diagnosis.*—The diagnosis was: congenital lymphangiectatic edema and lymphangiomatosis, generalized, especially marked in the skin of the right upper extremity, the right side of the neck, face and head, the left lower extremity and the left labia, the tongue, intestines and mesentery, with involvement of the regional lymph glands and with brawny edema in these areas; slight chylous ascites; slight hypertrophy and hyperplasia of the thyroid; slight anemia, moderate to considerable emaciation; slight acute enteritis; terminal hydropericardium (85 cc.); considerable edema of meninges; and pulmonary edema, especially on the right side.

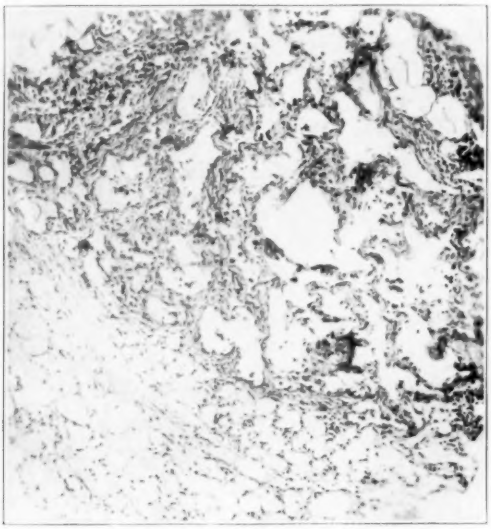

Fig. 9.—Mesentery (advanced stage). Dilated lymphatic channels, connective tissue overgrowth.

The probable cause of death was terminal hydropericardium and edema of the meninges in a case of congenital lymphangiectases and lymphangiomatosis (generalized).

## COMMENT

Reference to the embryology of the lymphatic system throws little light on the nature of the factors operating in the production of these lymphangiectases and the associated overgrowth of connective tissue. The lymphatic vessels and connective tissues are derived from the mesoderm, and it is apparently some developmental defect in this layer which is responsible.

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# OILS AND FATS

## THEIR ENTRANCE INTO AND FATE IN THE LUNGS OF INFANTS AND CHILDREN: A CLINICAL AND PATHOLOGIC REPORT *

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The six cases reported here have in common the occurrence in the lungs of a large amount of material of a fatty or oily nature. In attempting to determine as accurately as possible the source and nature of this material in each instance, it has become clear, beyond reasonable doubt, that its entrance into the lungs was by way of the trachea.

The literature on this subject is scanty. In 1920, Guieysse-Pellissier [1] studied the lungs of rabbits and dogs following intratracheal injections of olive oil. He found the alveoli filled with large mononuclear cells which had engulfed the oil (and which he considered as of epithelial origin), and also with polymorphonuclears and eosinophils. He thought that these epithelial cells contained lipase, and were capable of dissolving and absorbing the oil to a considerable extent. In 1922, Corper and Freed [2] published the results of intratracheal injections of chaulmoogra oil, olive oil and liquid petrolatum in rabbits. They found marked changes in the lungs from the injection of chaulmoogra oil, dependent partly on the chemical composition of the oil, but (of more concern to this report) they state that both olive oil and liquid petrolatum, similarly introduced, reached the alveoli, where they were "retained for a relatively long time (months) and where they can produce a mild type of proliferative bronchopneumonia." These workers did not describe the microscopic changes of the pulmonary condition in detail. They say: "It seems, so far as these studies have gone, however, that the reaction resulting in the lungs, especially to the more inert olive oil and liquid petrolatum, is to be attributed to a reaction which may to a great extent occur toward any foreign insoluble substance."

A recent article by Laughlin [3] of Toronto also deals with certain aspects of this question. Laughlin has reported four instances in which oil was found in the lungs in fairly large quantities, and a series of

* Received for publication, Sept. 17, 1926.

* From the pathologic laboratory of the Children's Hospital, and the Department of Pathology of the Harvard Medical School.

1. Guieysse-Pellissier: Recherches sur l'absorption de l'huile dans le poumon, Compt. rend. Soc. de biol. **83**:809 (May 23) 1920.

2. Corper, H. J., and Freed, H.: The Intratracheal Injection of Oils for Therapeutic Purposes, J. A. M. A. **79**:1739 (Nov. 18) 1922.

3. Laughlin, A. F.: Studies on Pneumonia Following Nasopharyngeal Injections of Oil, Am. J. Path. **1**:407 (July) 1925.

experiments on rabbits in which oil was introduced into the trachea and into the pharynx. Three of his cases occurred in young children and one in an adult who had paralysis of the larynx and vocal cords. He considered the material to be mineral oil in each case, and used only mineral oil in his animal experiments. He described the oil as occurring in large and small droplets, mostly within large mononuclear cells, and as being present only in the alveoli. His results suggested to him "that oil, by lowering the resistance of the tissues or by carrying infection from the nose and throat, may be a factor in the production of pneumonia." He pointed out that "the movements and final disposal of the oil phagocytes are subjects for further study." His conclusions are:

1. That oil finds its way into the alveoli of the lung, not only when directly introduced into the trachea, but also at times when administered in sufficient quantities in the nose and throat.
2. Oil when present in the lung is actively phagocytosed by endothelial cells which are present in sufficient numbers to dispose of all the oil present, and produce consolidation of the lung.

The cases here reported are of value because they show the sequence of events following the aspiration of oily substances. They have been numbered approximately in the order of their duration as estimated from the histologic picture. Briefly, it may be said that case 1 corresponds to the four cases reported by Laughlin. The other cases show increasing amounts of oil in the interstitial tissue of the lung, and case 6 shows practically an end-result—a firm nodular fibrosis of the lung, which on gross examination was suggestive of tumor formation, and microscopically was strikingly like the so-called "paraffinoma" produced by subcutaneous injection of oil. These cases also are different from those reported by Laughlin in that the material in the lungs apparently was mineral oil in only three of six patients. They are reported because they seem to indicate that the condition is not uncommon (six cases occurring in 290 consecutive necropsies), and that it is of considerable practical importance.

## CASE REPORTS

CASE 1.—*History.*—A boy, aged 3 months, was admitted to the hospital, July 16, 1924, because of irritability and fever. The family history and the past history were irrelevant. The infant weighed 7¼ pounds (3,182 Gm.) at birth, was successfully fed on an artificial formula, and weighed 10 pounds (4,535 Gm.) at entry. Four days before admission to the hospital, he sneezed several times. The next day he coughed a little. Two days before the entry he had a nasal discharge and the local physician prescribed cough medicine and nose drops (of unknown nature). The infant's temperature was found to be 102 F. The next day the respirations were rapid, and the child was admitted to the hospital.

*Course in Hospital.*—The child was too ill for a complete physical examination. There was bronchial breathing at both bases, with showers of râles all over the chest. The infant died the day following admission, five days after the onset of illness. The clinical diagnosis was lobar pneumonia.

*Necropsy.*—Two hours after death, necropsy was performed. The nourishment and development of the child were fair. The only observations relevant to this study were noted in the lungs. The right lung weighed 38 Gm., the left weighed 34 Gm., and both were alike in appearance. The organs were voluminous and held their shape instead of collapsing when placed on the table. This was particularly noticed in the posterior upper lobe, in which the parenchyma stood out like liver tissue. These areas were firm and rubbery. The external surfaces were smooth, moist, glistening and pale yellow-gray, mottled with a few small reddish areas. The cut surface showed large areas of consolidation. When pressure was applied to these pneumonic areas, thick creamy pus came from the bronchioles and no fluid or air from the adjacent parenchyma. Fully five sixths of the lung tissue was involved in this process. There were no evidences of tuberculosis. The lower lobes were less involved than the upper lobes.

*Anatomic Diagnosis.*—Acute bronchitis, bronchopneumonia with lobar distribution and early acute peritonitis were diagnosed.

*Microscopic Description.*—The alveolar spaces and bronchioles were filled with a cellular exudate composed of polymorphonuclears, large mononuclears, with a few lymphocytes and red cells and a small amount of fibrin. In many areas there were only a few polymorphonuclears in the alveoli, and the bulk of the exudate was composed of large mononuclear phagocytes which contained many oil droplets, varying in size from 2 to 30 microns. A few larger droplets (45 microns or more in diameter) appeared to lie free in the alveoli. There was no foreign body giant cell reaction. The oil droplets were rarely seen in the bronchioles. A few large mononuclear phagocytes, laden with many small oil droplets, were seen in the lymphatic vessels in the walls of the alveolar ducts and in the peribronchial lymphatics, but the great bulk of the oily material had not left the alveoli. This was consistent with the short length of time (from three to four days) which had elapsed since the probable date of aspiration of the material. The other organs showed some evidences of septicemia, but no other important changes.

*Microscopic Diagnosis.*—Microscopic examination revealed acute bronchitis and bronchopneumonia, aspiration of an oily material (probably mineral oil), early acute peritonitis and acute diffuse hepatitis (early).

Case 2.—*History.*—A boy, aged 7 months, was admitted to the hospital, Aug. 20, 1925, with the complaint of diarrhea and vomiting. The family history was unimportant. The infant was breast fed for three weeks, and then fed (rather unsuccessfully) on various formulas. For several months he had been given cod liver oil, at first only 3 drops three times daily, and later in much larger quantities (at least one-half ounce [15 cc.] daily). The present illness began four days before entry, with vomiting, diarrhea and rapid respirations, associated with some coughing and sneezing. Recently the infant had become weak and drowsy. On physical examination, he was sickly looking and restless; his face was flushed, and the lips were dry and wrinkled. The nasopharynx was injected. The chest showed a slight rosary. Increased tactile fremitus, and slight dulness over the entire right lung were noted. The breath sounds over the right lung were fainter than those over the left.

*Course in Hospital.*—The infant showed a daily rise in temperature of from 103 to 105 F. The urine showed sugar on three examinations and acetone bodies on the first examination only. The blood was essentially normal. The Wassermann reaction and tuberculin tests were negative. Otitis media developed and was treated by paracentesis; later mastoidectomy was performed. A few days before death (which occurred one month after entry), many râles were heard throughout both lungs. While the patient was in the hospital, no oily material was administered.

*Clinical Diagnosis.*—Acidosis and vomiting, diarrhea, and bronchopneumonia were diagnosed.

*Necropsy.*—Necropsy was performed two hours after death. The nourishment and development were fair. Observations other than those in the lungs were unimportant.

The right lung weighed 84 Gm. and the left, 45 Gm. Both lungs were rather uniformly reddened and noncrepitant, and on section were reddish purple, mottled with white, confluent areas of slightly increased density. This mottling was most striking in both upper lobes.

*Anatomic Diagnosis.*—Bronchopneumonia, mastoiditis (right), postoperative, otitis media (bilateral), and slight fibrinous pericarditis were diagnosed.

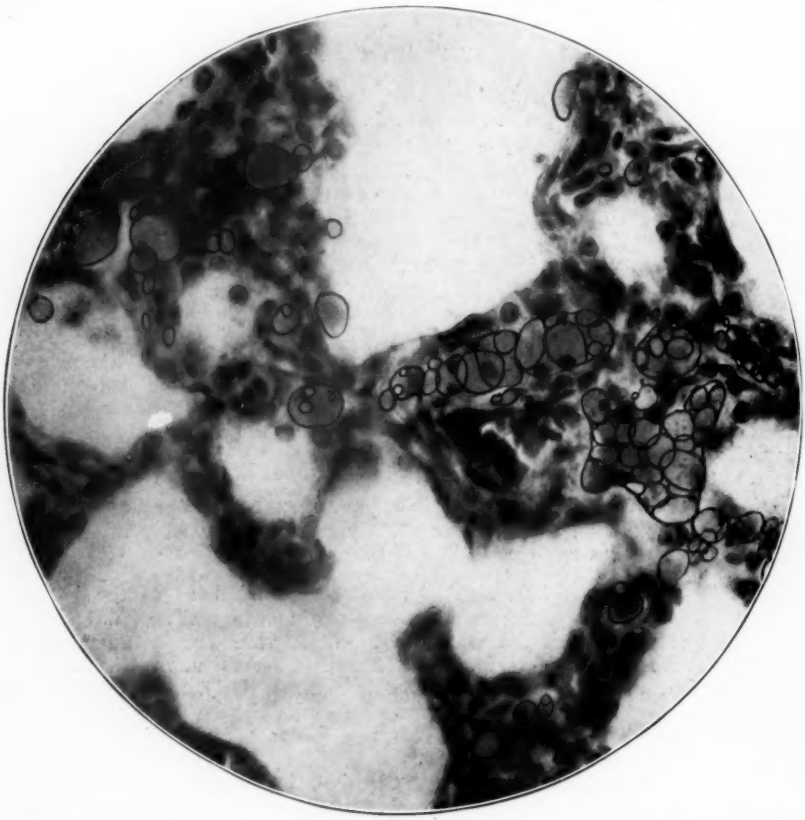

Fig. 1 (case 2).—Frozen section of lung, stained with scharlach R-hematoxylin. Oil droplets may be noted in the alveolar walls. The alveoli are clear. The oil droplets have been outlined with ink.

*Microscopic Description.*—The alveoli and bronchioles in many large areas were filled with a purulent exudate. Large numbers of oil-laden large mononuclear phagocytes were also present in most of the alveoli and in the walls of the alveoli and alveolar ducts. Many of the alveoli were lined with cuboidal epithelium which appeared to be desquamating, but these fixed epithelial cells contained no oil. Oil vacuoles were also numerous in the peribronchial lymphatic vessels. Oil droplets were not seen in the bronchioles. Clumps of bacteria were numerous. One section showed a layer of fibrinopurulent exudate on the pleural surface. The staining reactions of the oily material in the lungs

can be seen in the table. Sections of the other organs showed no changes of importance to this study.

*Microscopic Diagnosis.*—Bronchopneumonia and aspiration of oil (probably cod liver oil) were diagnosed.

CASE 3.—*History.*—A colored boy, aged 6 months, was admitted to the hospital, Nov. 28, 1925, because of convulsions since birth. The family history was unimportant. The infant was born at full term; delivery was normal. The birth weight was 6¾ pounds (3,011 Gm.). He was breast fed for one month, then was given a proprietary food for one month and then malted milk for one

Fig. 2 (case 3).—Frozen section of lung, stained with scharlach R-hematoxylin. The alveoli are lined with cuboidal epithelium, and contain mononuclear phagocytes with ingested fat droplets. The alveolar walls are widened and infiltrated with fat-laden mononuclears. The fat droplets are outlined with ink.

month. For the rest of the time previous to entry, a formula prescribed by the outpatient department of the Children's Hospital was given. The infant had had repeated convulsions since the age of 2 months. These lasted for five minutes, involved the arms, legs, face and eyes, and did not respond to calcium chloride therapy. Chvostek's and Trousseau's signs were positive. Three weeks before entry the infant was brought to the outpatient department because of a severe cough, and the condition was diagnosed as bronchopneumonia without

elevation of temperature. Roentgen-ray examination showed consolidation in the left cardiohepatic angle. The cough continued until the infant entered the hospital. No history of the use of fatty or oily substances other than milk could be obtained. On entering the hospital, the infant was stuporous, breathing rapidly, and cried and coughed when disturbed. There was dulness and bronchial breathing at the base of the left lung. There was slight enlargement of the costochondral junctions and wrists. The blood calcium was 7.6; the blood phosphorus, 2.9. Urinalysis showed a heavy trace of albumin on one occasion and sugar on two out of three examinations. The blood counts were normal. The Wassermann and tuberculin reactions were negative.

*Course in Hospital.*—The infant remained stuporous and was fed by gavage during his entire stay in the hospital (three weeks). The course was practically afebrile until the last three days, when the temperature rose suddenly and the infant died. The diagnosis of bronchopneumonia, made in the outpatient department, was not confimed while the baby was in the hospital. No fatty or oily substances other than milk were given while the baby was in the hospital.

*Clinical Diagnosis.*—Birth injury and tetany were diagnosed.

*Necropsy.*—Necropsy was performed three hours postmortem. The development and nourishment were fair. The feet were extended in the position of carpopedal spasm. There was a moderate rosary. The right lung weighed 90 and the left 85 Gm.; externally they were pinkish yellow, shading to deep red at their bases. On palpation, they were distinctly less crepitant than normal and felt firm, especially in their lower lobes. On section, they were pale yellowish gray, mottled with a few hemorrhagic areas, but no sharply localized areas of consolidation were made out. The entire cut surface, especially in both lower lobes, was distinctly firmer and drier than normal, and on pressure only a small amount of froth exuded. A definite purulent exudate was expressed from the bronchioles. The lymph nodes at the hilum were slightly enlarged. The bronchial mucosae were covered with a mucopurulent exudate. The pulmonary vessels were normal. The other organs appeared essentially normal, except for the brain, which showed marked injection and diffuse old hemorrhage into the pia-arachnoid, and some questionable atrophy of the frontal lobe convolutions.

*Anatomic Diagnosis.*—Bronchopneumonia, rachitis (mild), diffuse old hemorrhage in the pia-arachnoid and atrophy of the frontal convolutions were diagnosed.

*Microscopic Report.*—The only observations of importance were noted in the lungs. These presented a remarkable picture. In many sections, every alveolus was lined with cuboidal epithelium, and the alveolar walls were so distended that they appeared wider than the alveoli. This distention of the alveolar walls was seen to be due to large numbers of mononuclear phagocytes laden with fat droplets, which averaged somewhat smaller than the globules seen in the other cases, being from 2 to 12 microns in diameter as a rule. These fat laden mononuclear cells were also present in most of the alveoli. The alveoli also contained a liquid material which was slightly eosinophilic. Occasionally moderate numbers of polymorphonuclear cells were seen in the alveoli, but the bronchioles often contained a definite purulent exudate. Only a few small fat droplets were seen in the bronchioles which contained this exudate. In some sections, the lung tissue appeared normal, and the alveoli were lined with normal platelike respiratory epithelium. In these areas, no fat laden cells were present, either in the alveoli or in the alveolar walls. One section showd a sharp line of demarcation between the normal and the involved lung tissue, a thin interlobular septum intervening.

*Microscopic Diagnosis.*—Acute bronchopneumonia, fatty material (probably milk) in alveoli and alveolar walls, cuboidal alveolar epithelium, rachitis (mild), meningeal hemorrhage and cerebral congestion were diagnosed.

CASE 4.—*History.*—A boy, aged 10 months, was admitted to the hospital, Oct. 22, 1924, in order to solve the problem of feeding him. His family history was unimportant. The infant was born at full term; delivery was normal.

The birth weight was 8¾ pounds (3,912 Gm.). He was breast fed for one week only, then put on various formulas, all of which proved unsuccessful. The infant had a severe upper respiratory infection at the age of 3 months. The local physician had made a diagnosis of rachitis, and for four months previous to admission the infant had been given 15 drops of cod liver oil three times daily. On admission, the infant was much undersized, poorly developed and undernourished, weighing 7½ pounds (3,373 Gm.), or 1½ pounds (674 Gm.) less than at birth. The abdomen was prominent.

*Course in Hospital.*—The treatment consisted in attempting to improve the state of nutrition by proper feeding. For ten days the infant was given the yolk of one egg daily in his milk modification, which consisted of whole lactic

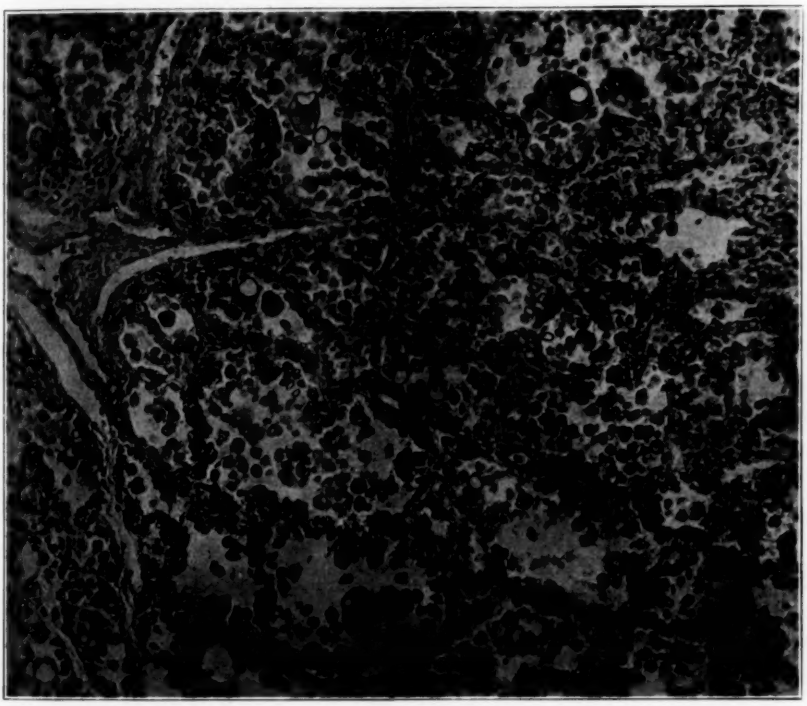

Fig. 3 (case 4).—Paraffin section of lung stained with hematoxylin and eosin. The alveoli are filled with mononuclear phagocytes and giant cells containing oil droplets (outlined with ink). A few polymorphonuclears are seen. A slight thickening of the alveolar walls is present.

acid and corn syrup (he was not fed by gavage while in the hospital, as far as could be ascertained). He was then given Czerny's butter-flour mixture for five days, and then protein milk for a week. On all of these formulas he failed to gain satisfactorily, and was put back on lactic acid milk, with the occasional substitution of breast milk when possible. Urinalysis was negative. The white cell count was normal until three days before death, when it rose to 30,000 (53 per cent polymorphonuclears, 31 per cent lymphocytes, and 16 per cent large mononuclears). Other observations were: red cell count, 4,240,000; hemoglobin content, 70 per cent.; blood calcium, 9.4 mg.; blood phosphorus, 4.0 mg.; serum protein, 6.93. The Wassermann and tuberculin tests were negative. The stools were often soft and yellow. No chemical examination of the

stools was made. Nine days before death the infant developed a severe cold, and a few days later râles and rhonchi were heard throughout both lungs, and a diagnosis of bronchopneumonia was made. The infant died on Dec. 30, 1924, having been in the hospital for six weeks. During the last three days of life, he was treated with nose drops every three hours, of the following composition: epinephrine inhalant, 1 ounce (31.1 Gm.), olive oil, 1 ounce (31.1 Gm.).

*Clinical Diagnosis.*—Chronic malnutrition and bronchopneumonia were diagnosed.

*Necropsy.*—Necropsy was performed seven hours postmortem. The body was markedly emaciated; the skin was dry and inelastic. Subcutaneous fat was absent. The head appeared large, and the anterior fontanel measured 6 by 2 cm. The abdomen protruded markedly. The right lung weighed 32 Gm.; the left, 20 Gm. Both lungs were similar in appearance and collapsed when placed on the table. The external surface was smooth, glistening and salmon pink, mottled with areas of red. On palpation the parenchyma was soft and crepitant for the most part, but here and there were small firm areas which were deep red. These areas numbered about ten in all, and were usually about 1 cm. in diameter. The cut surface was for the most part salmon pink, mottled with these red areas, which had indistinct borders. On pressure, frothy fluid exuded from the red areas, which, however, appeared increased in density. Pus was expressed from the bronchioles. Pulmonary vessels were negative. Lymph nodes at the hilum were not enlarged. There were no evidences of tuberculosis.

The other gross observations, which are considered to be unrelated to those in the lungs, may be summarized as follows: The pancreas weighed 8 Gm., was markedly fatty and soft, and did not show normal lobulations. The pancreatic duct could not be probed. There was chronic fibrous perisplenitis and chronic fibrous perihepatitis. The costochondral junctions were enlarged.

*Anatomic Diagnosis.*—Fatty degeneration of the pancreas, malnutrition, rachitis, bronchopneumonia, fatty liver and chronic fibrous perisplenitis and perihepatitis were diagnosed.

*Microscopic Description.*—The alveolar walls were frequently thickened and showed a connective tissue increase. Other alveolar walls were thin and delicate, while still others were tortuous, congested and contained many polymorphonuclear cells. The alveoli in some areas were atelectatic; in other areas they were somewhat emphysematous. The alveolar spaces frequently contained countless mononuclear leukocytes. In many instances, these were forming and had formed giant cells. Ofter, large, circular, yellow structureless bodies that resembled fat or oil globules were present. These had not been dissolved in the regular paraffin sections fixed in Zenker's solution, and still stained bright red with scharlach R. These globules were situated not only in the alveoli, but also in the walls of the alveolar ducts and in the peribronchial and periarterial lymphatic channels. They were mostly within large mononuclear and giant cells, but occasionally were free. In other parts many polymorphonuclear cells were present with the endothelial leukocytes within the alveoli. Bronchioles often contained plugs of fibrinopurulent exudate. Not infrequently, the bronchial wall was necrotic and the process extended into adjacent alveoli. The interlobular and interlobar septums were often wide and dense, giving a great deal of connective tissue to the organ. The pancreas was represented by fatty tissue, embedded in which were fairly normal islands of Langerhans, surrounded by a few atrophic acini. The liver showed a diffuse cirrhosis.

*Microscopic Diagnosis.*—The diagnosis was: acute purulent bronchitis, acute peribronchitis, bronchopneumonia, foreign body reaction in lungs to lipoid substance, fibrosis of lung, pulmonary thrombosis (?), acute splenitis, fatty degeneration of pancreas (severe), cirrhosis of the liver, old pyelitis, rachitis (?) and osteomalacia (?).

NOTE.—The observations in the pancreas and liver undoubtedly explain this infant's failure to assimilate food. The underlying etiology of this condition,

whether congenital or acquired, has not been determined, but the case, together with several other similar cases, is still being studied.

CASE 5.—*History.*—An infant, aged 5 months, was admitted to the hospital, May 1, 1924, because of cough and rapid respirations. The family history was negative. The infant was born at full term, and delivery was normal. The infant was always breast fed. Cod liver oil or orange juice was never given. The infant had a slight cold at the age of 3 months, which lasted for one week. Otherwise, there were no other illnesses, but the patient was always weak and under nourished. Two days before entry, the baby began to cough and breathe rapidly.

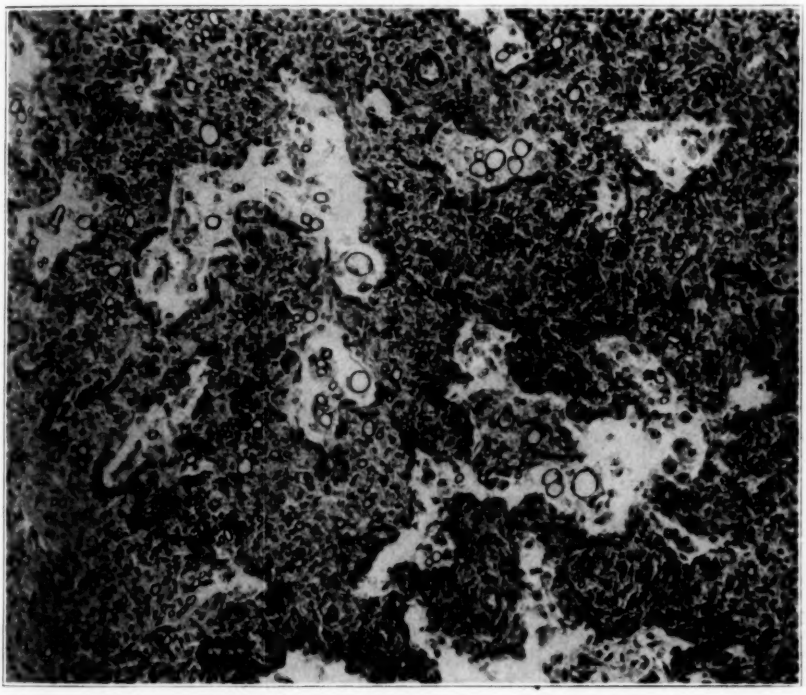

Fig. 4 (case 5).—Paraffin section of lung stained with hematoxylin and eosin. There is marked fibrosis of the alveolar walls; much finely divided oil is present in this fibrous tissue. The alveoli are compressed and contain oil-laden mononuclears. The oil vacuoles are outlined with ink.

*Physical Examination.*—Emaciation and rapid respirations were present. A marked rosary was noted. There was impaired resonance throughout both lungs, especially over the left lower lobe and in the left axilla. Coarse squeaks and scattered râles were present throughout. The spleen was palpable. A roentgenogram showed some mottling of the right cardiohepatic angle and partial right-sided pneumothorax, which disappeared in one week.

*Course in Hospital.*—The temperature rapidly dropped from 104 F. to normal, and remained so, but a loose productive cough persisted, together with coarse bronchial râles. The Wassermann reaction and the tuberculin test were negative. Urinalysis and examinations of the blood showed nothing remarkable. Four weeks after entry the infant was discharged, apparently well.

*Readmission.*—Seven weeks after discharge, July 21, the child was readmitted with a severe productive cough. Physical examination showed undernourishment as before; the skin was grayish and slight cyanosis was present. There was dulness over the upper right part of the chest, with bronchial breathing, medium moist râles and bronchophony.

For three or four days the temperature was nearly normal, but then rose again, and the lung signs became more evident. The infant was given 1 cc. of cod liver oil by mouth daily for the first two weeks, and 4 cc. daily for the last ten days. Four cubic centimeters of mineral oil was also administered by mouth every day during this entire period. The infant died three and one-half weeks after admission.

*Clinical Diagnosis.*—Bronchopneumonia was diagnosed.

*Necropsy.*—This was performed one hour postmortem. The body was extremely emaciated; the abdomen was distended. The right lung appeared small and weighed 44 Gm. Its upper lobe was dark red and airless. Small, firm grayish-white masses about 1 mm. in diameter were seen beneath the pleura. The sectioned surface was uniformly dark red. A few of the small grayish-white masses were deep in the tissue. No pus was expressed. The pleural surface was stained brown, giving the impression of old blood. The sectioned surface was less pigmented. The left lung weighed 28 Gm. It had two atelectatic portions—a small area at the base and a large area in the upper and posterior aspect of the upper lobe. These areas had none of the firm gray granules in them. The remainder of the postmortem examination was unimportant.

*Anatomic Diagnosis.*—Emaciation, bronchopneumonia, atelectasis and tympanites were diagnosed.

*Microscopic Description.*—The bronchioles were often filled with purulent exudate, and in many instances this exudate was being organized. A few of the surrounding alveoli occasionally contained a purulent exudate, but this was not a striking feature in any of the sections examined. The peribronchial tissues also showed a moderate infiltration with lymphocytes, polymorphonuclears, and large mononuclears, which were often present in the lymph channels. The alveoli were collapsed in many areas, but were almost uniformly filled with large mononuclear cells and giant cells, which had engulfed large globular masses, shown by scharlach R. and other stains to be of a fatty or oily nature. A few of these globules were apparently free, but the great majority of them were intracellular. Some of the larger ones, measuring from 35 to 40 microns in diameter, were only partially surrounded by giant cells. These fatty or oily globules were not found in the exudate in the bronchioles, probably because they had been removed from this location by the action of the cilia. The alveolar walls in nearly all of the lung tissue included in the sections were greatly thickened, often being wider than the alveoli. In many areas, this thickening was due partly to the presence of innumerable droplets of the same material seen in the alveoli, but usually in rather smaller masses, averaging about 10 to 15 microns in diameter. The same material was also abundant in the peribronchial and perivascular lymphatic channels, which showed endothelial proliferation, often to an extreme degree. Scharlach R stains showed no oily droplets in the fixed bronchial epithelial cells. In other areas, the thickening of the alveolar walls appeared to be due to an increase in fibrous tissue and in the number of endothelial cells. In a few instances, connective tissue had obliterated the alveoli.

In two of the sections, there was an extraordinary degree of increase in the peribronchial and perivascular lymphoid tissue, and isolated lymph follicles were seen which appeared to be in the walls of the alveolar ducts. These lymph follicles often showed the hyalinzed centers and phagocytosis of nuclear débris by large mononuclear cells, which appearance was described by Mallory as a toxic manifestation. These lymph nodules were most numerous just

beneath the pleura, and undoubtedly represented the small grayish-white masses, about 1 mm. in diameter, which were so striking in the gross appearance. The sections of the other organs were essentially negative.

*Microscopic Diagnosis.*—Chronic obliterating bronchitis, fibrosis of the lung, foreign body giant cell reaction to aspirated oily material and early acute colitis were diagnosed.

CASE 6.—*History.*—A boy, aged 6 years, whose early history was not known, except that he was an only child of parents 36 years old, and was born at full term, instrumental delivery, at the age of 13 months was seen by Dr. Karlton Percy, who found him underweight, nervous and constantly making athetoid

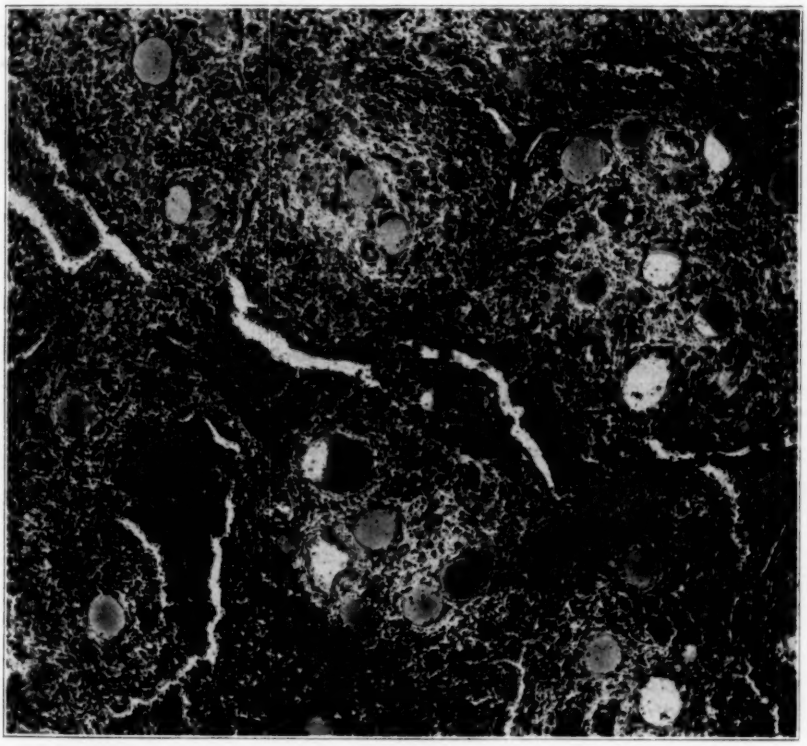

Fig. 5 (case 6).—Frozen section, stained with scharlach R-hematoxylin, from the center of a large fibrous nodule in the lung. Oil droplets are embedded in fibrous tissue and surrounded by giant cells. Heavy lymphocytic infiltration may be noted. Note the tubercle-like structure in the upper central portion of the figure.

movements. There seemed to be a marked carbohydrate intolerance. At the age of 2 years, the child was seen by Dr. Bronson Crothers, who made a diagnosis of spastic paraplegia due to birth injury; he thought the lesion was probably extrapyramidal. At the age of 2 years and 3 months, the child had acute otitis media, and at 3½ years severe pneumonia, with marked cerebral symptoms, and barely escaped death. The condition of the central nervous system improved slowly with muscle training. The last illness occurred when the child was 6 years old. Eight days before death bronchitis developed, with

an elevation of temperature to 103 F. The temperature came down to normal in a few days, but eventually rose again, and the child died.

At various times during his life, this child was given pink nose drops consisting of iodine and menthol in liquid petrolatum. He also was given liquid petrolatum once, two or three times weekly for a considerable period (the amount of the latter administered was not definitely known).

*Necropsy.*—This was performed eight hours postmortem at the Harvard Medical School, on March 1, 1926. The body was fairly well nourished. The peritoneal cavity was essentially normal except for the mesenteric lymph nodes. These were moderately enlarged, and on section presented a somewhat unusual

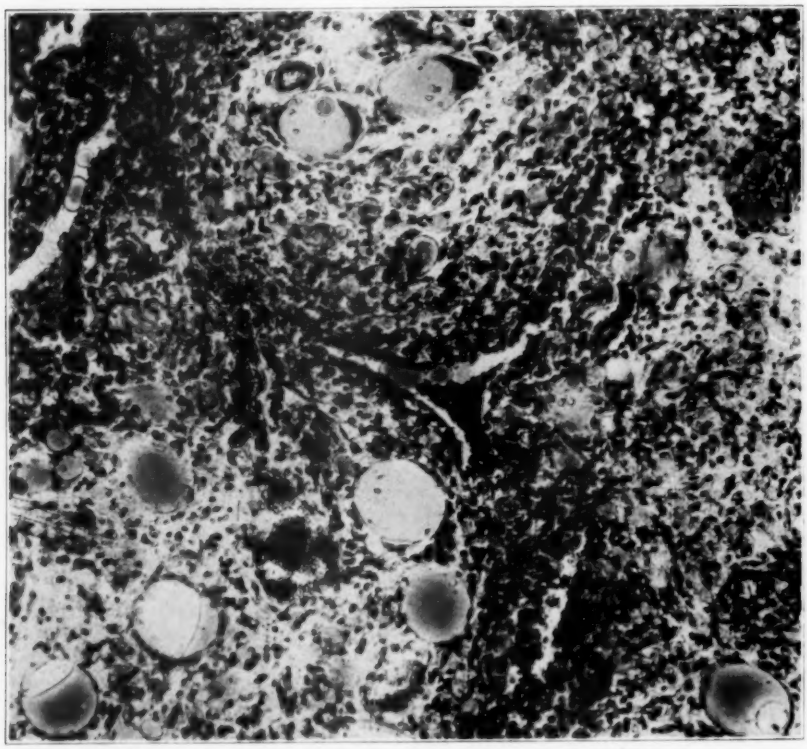

Fig. 6.—Higher power magnification of a portion of the field in figure 5. The triangular structure in the center probably represents a compressed alveolus or bronchiole.

appearance. Most of the larger lymph nodes, on section, were grayish pink, and appeared to be of normal consistency. Four or five of the medium-sized lymph nodes, on the contrary, were opaque yellowish white, both externally and on section; their consistency seemed considerably firmer than that of normal lymph nodes, and was definitely firmer than that of the adjacent lymph nodes. The cut surface of these nodes was homogeneous and opaque yellowish white, but there was no evidence of caseation and no evidence of an inflammatory process around the capsule. In the right pleural cavity, corresponding to the outer and anterior portion of the right lower lobe, was an area of pleural adhesion 3 or 4 cm. in greatest dimension. These adhesions were fairly easily broken. The pericardial cavity was normal. The heart was essentially normal except for pallor and dilatation of the right auricle.

The lungs were the seat of marked changes. The pleural surfaces were reddish pink, mottled with many areas of deep reddish purple and several areas of dark bluish discoloration. To palpation, in both lower lobes, and to a lesser extent in the right middle and upper lobes, the lung substance felt definitely nodular, the nodules being from 1 to 3 cm. in diameter. On section, these nodular areas were seen to be opaque yellowish white, and extremely firm in consistency, so as to give the impression of a tumor at first glance. The largest of these nodules was located in the upper portion of the right lower lobe. It was about 3 cm. in diameter. The nodules were fairly sharply demarcated

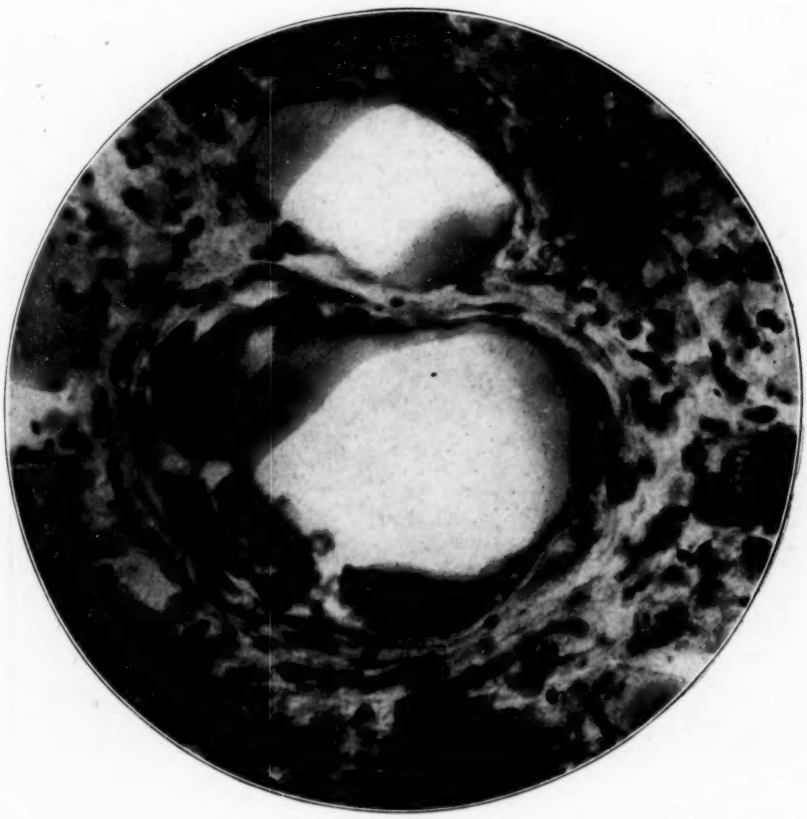

Fig. 7 (case 6).—Frozen section of lung, stained with scharlach R-hematoxylin. Concentric fibrosis and giant cell formation around a large drop of oil.

from the surrounding lung tissue in many instances, but occasionally they seemed to blend with the lung tissue. Pressure on the cut surface of one of these nodules caused a small amount of inspissated yellowish-white material to exude in minute plugs. A frozen section was made of a portion of this solidified lung substance, and it gave the impression of an extensive organized inflammatory process rather than of a tumor. This process of solidification appeared to have involved nearly one half of the entire lung substance, and even in the uninvolved areas there seemed to be a definite increase of the fibrous tissue around the bronchioles. There was no gross evidence of an acute pneumonic process. The bronchial lymph nodes were definitely enlarged, deep red externally, and on section the cut surface varied from deep red to reddish

gray, and in many areas was mottled with minute grayish-white areas about 1 mm. in diameter, which were thought to represent the lymph follicles. The bronchial mucosa was slightly injected, and presented a very small amount of thin mucinous material. The pulmonary vessels were normal.

The spleen appeared slightly enlarged, and its edge was slightly rounded. Its capsule was smooth and translucent. On section, it was deep red, and the pulp was fairly easily scraped away with the knife. Thin sections, however, were cut easily. The malpighian corpuscles were numerous, and presented a rather unusual appearance in that each one was surrounded by a definite hemorrhagic ring, while the central portion of the corpuscle was opaque grayish-white.

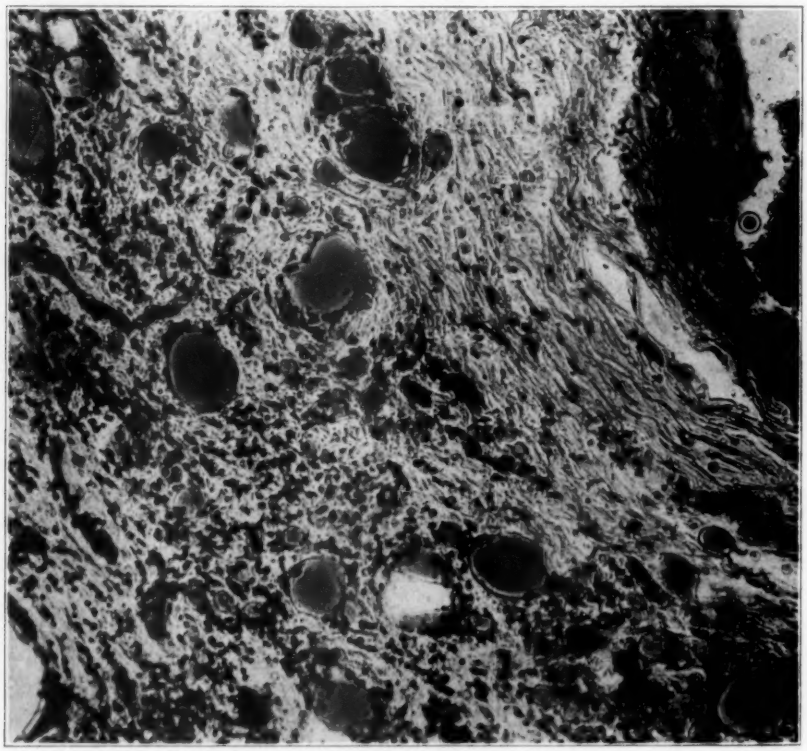

Fig. 8 (case 6).—Frozen section of lung, stained with scharlach R-hematoxylin. The peri-arterial lymphatics are distended with oil. Proliferation of lining endothelium is present.

The pancreas was normal. The liver was normal except for some yellowish mottling. The gallbladder was normal; the bile ducts were patent. The kidneys were essentially normal; there was slight dilatation of the left pelvis and of both ureters. The bladder, suprarenals and aorta were normal. The genitalia showed bilateral undescended testicles, the left being in the pelvis and the right in the inguinal canal. The brain showed moderate edema and congestion. It was given to the department of neurology for special study of the central nervous system condition responsible for the spastic paraplegia. This study has not been completed, but is not relevant to this report. The right middle ear cavity contained a small amount of purulent material.

*Anatomic Diagnoses.*—Organized inflammatory process in the lungs; bilateral hydro-ureter, dilatation of the pelvis of the left kidney, undescended testicles, edema and congestion of the brain and otitis media on the right were diagnosed.

*Microscopic Description.*—Sections were stained with hematoxylin-eosin, eosin-methylene blue, by Giemsa's method, with Weigert's connective tissue stain, iron hematoxylin, and with the various stains for fatty substances. The heart was essentially normal. No fat or oil could be demonstrated except in the epicardium. Sections taken through the nodular areas described grossly showed the normal lung tissue to be virtually replaced by a loose connective tissue framework to such an extent that it was almost beyond recognition. This connective tissue, by ordinary staining methods, appeared interspersed with countless vacuoles, varying in size from that of a red cell or smaller to nearly that of a normal lung alveolus. Frozen section stains on formaldehyde material showed these vacuoles to contain an oily or fatty substance, which stained bright orange-red with scharlach R, light pink with nile blue sulphate, and was not stained with osmic acid (with or without subsequent alcohol treatment). Prolonged fixation in potassium dichromate at 50 C. did not prevent the material from being dissolved out later by fat solvents. The substance was not doubly refractive when viewed through Nicol prisms, as noted in the table.

This tissue had somewhat the appearance of normal adipose tissue in some areas, except that the fat globules showed more variation in size. In many instances, the larger masses of globular material were surrounded by large mononuclear phagocytes, which had coalesced to form foreign body giant cells. In some areas, one saw large mononuclear phagocytes which contained many small globules.

The determination of the exact location of the fatty material with reference to the anatomic elements of the lung offered the greatest difficulty, owing to the almost complete departure of the microscopic picture from that of a normal lung. In the central portions of the consolidated areas were large areas in which no traces of alveolar walls or bronchioles could be made out. Weigert's elastic tissue stain in such areas showed complete absence of elastic fibrils. In other areas, a few short irregular elastic fibrils were made out, and in the uninvolved areas elastic fibers were normal in appearance.

Sections passing through the margin of the consolidated portions yielded more information regarding the location of the oil. Here alveolar walls were seen which were many times the normal thickness, and which contained many oil globules, some of which were within large mononuclear cells, while others (larger, as a rule) were free. In places also the alveoli appeared compressed, as though by progressive distention of the alveolar walls. This appearance seemed to indicate that the oil deposition and fibrosis took place primarily in the walls of the alveolar sacs and alveolar ducts rather than within the air spaces.

The connective tissue which had thus overgrown the lung tissue was heavily infiltrated with lymphocytes, large mononuclears and a few eosinophils and polymorphonuclears. In a few areas, chiefly in the more nearly normal portions, bronchioles and alveoli were filled with a frankly purulent exudate. The connective tissue was rich in capillaries, which were well engorged, but in many areas the alveolar walls were outlined as zones of increased vascularity. There had been some proliferation of the bronchial epithelium in places, and numerous alveoli were lined with cuboidal epithelium.

In some places, the margin between the involved and uninvolved lung substance was sharp, and essentially normal lung tissue was seen close to the lung tissue in which there was complete fibrosis such as has been described in the foregoing. More often, however, the uninvolved lung substance was markedly atelectatic; there was extreme distention of the alveolar wall capillaries with red cells, and the compressed alveoli were filled with serum.

In one section, representing an area of atelectasis and congestion with little or no fibrosis, numerous irregular, vermiform masses, staining deep bluish black

with hematoxylin, were seen. These resembled calcium deposits. Great numbers of hemosiderin-laden large mononuclear cells were also present here.

The capsule and trabeculae of the spleen were normal. There was marked congestion in the form of hemorrhagic zones around the malpighian corpuscles. Malpighian corpuscles were numerous and appeared normal. Here and there, nearly always around small blood vessels, or within or close to lymph follicles, were small groups of fatty or oily globules, embedded in a loose connective tissue framework similar to that seen in the lung. The fatty material gave exactly the same staining reactions as that in the lung. There was moderate proliferation of the reticular endothelium. There was a definite increase in polymorphonuclears in the pulp, especially in more or less focal areas.

In the pancreas, there was some hemorrhage into the capsule. Acini, islands and duct structures appeared quite normal. Fat stains showed only rarely a fat cell in the connective tissue about the ducts.

In the gastro-intestinal tract, the gastric mucosa showed petechial hemorrhages and staining abnormalities in the superficial layer, which were probably largely of postmortem origin. Similar changes were seen in the mucosa of the ileum in some sections.

In a few areas, the liver cord cells showed pale-staining cytoplasm, and vesicular nuclei. In focal areas the sinusoids contained moderate numbers of polymorphonuclears, which in rare instances were invading liver cord cells. Portal areas and bile duct structures appeared normal. The Kupffer cells were normal. The sinusoids were moderately congested in some areas. The liver cord cells contained only moderate numbers of small fat vacuoles, which stained deep black with osmic acid.

The suprarenals were essentially normal except for some increased vacuolization of the cortical cells, especially those in the superficial layer. The fatty material in the cortical cells stained bright red with scharlach R, and deep blue with nile blue sulphate. It was doubly refractive when viewed through Nicol prisms. The medulla contained practically no fatty material.

The glomerular tufts of the kidneys contained an increased number of polymorphonuclear cells. The tubular epithelium showed staining abnormalities consistent with postmortem change. No visible fat could be demonstrated in the tubular epithelium or elsewhere in the kidney substance.

One section of the thymus appeared entirely normal.

Lymph follicles of the mesenteric lymph node were few in number and showed a slight toxic reaction in their centers. There was considerable endothelial proliferation, but no definite fibrosis. No oil or fat vacuoles were noted.

The bronchial lymph nodes showed intense congestion. Malpighian corpuscles were few in number and showed a marked toxic reaction in their centers. The peripheral sinuses and lymph channels contained many large mononuclears, which often contained oil droplets. Eosinophils and polymorphonuclear cells were rarely encountered. There was marked endothelial proliferation. One also saw, here and there, groups of oil globules (both intracellular and extracellular). The oily material found here gave the same staining reactions as that in the lung, and was not doubly refractive. There was little or no connective tissue increase.

One section of a rib showed the marrow spaces filled with normal blood-forming marrow.

*Microscopic Diagnosis.*—The diagnosis was: chronic inflammation of the lung, with extreme fibrosis and foreign body giant cell reaction to an oily material (probably mineral oil); oil deposition in the lungs, bronchial lymph nodes and spleen (slight); chronic bronchial lymphadenitis; acute bronchiolitis and bronchopneumonia; acute splenitis; petechial hemorrhages in the mucosa of the stomach and the ileum and early focal necrosis of the liver.

ORIGIN OF THE MATERIAL IN THE LUNGS

When these cases were first studied, the possibility of oil or fat aspiration presented itself as a simple and probable explanation. Because of the interstitial location of a large part of the material, however, and because of associated pathologic conditions in two cases, it was thought necessary to entertain and rule out several other possibilities as far as possible.

In case 4, because of the definite pancreatic insufficiency, it was thought that the material might have originated from the chyle, and have been deposited in the lungs, owing to some metabolic disturbance. Gilbert and Jomier [4] and others have reported the presence of large globoid masses of fat in the lungs of normal dogs. They believe that the fat arrives in the lungs by way of the pulmonary arteries, and forms large coalescent blocks in the alveolar wall capillaries. Part of this fat, according to their conception, passes out through the pulmonary veins, part is consumed in situ and a part reaches the alveoli by rupture of the alveolar walls, and is eliminated by way of the bronchi. The large masses of fat are extracellular, and they do not describe any foreign body giant cell reaction or fibrosis. The amount of fat which they describe in the lungs is much smaller than that in the cases here reported.

Busquet and Vischniac [5] injected olive oil into the saphenous veins of dogs, and concluded (by chemical examination of the various organs) that more than 90 per cent of the injected oil came to rest in the lungs within a short time.

This question of the occurrence of fat in the normal lung and its relation to fat embolism is of great interest and deserves further study, but it is thought that such an explanation has been fairly definitely excluded in the instances reported here.

A similar explanation to that just mentioned was entertained in case 2, because of the severe acidosis and consequent possibility of a lipemic condition of the blood. There was, however, no definite evidence that lipemia did exist in any of these instances. Moreover, when, as in diabetes, lipemia does occur of such severity that fat-laden cells are deposited in the spleen, no such appearance has ever been described in the lungs.[6]

In the second place, it seemed remotely possible that the fatty material might have had its origin in the lung itself. In any pneumonic

4. Gilbert, A., and Jomier, J.: Compt. rend. Soc. de biol. **59**:87, 1905; Summary of Previous Work, Paris méd. **1**:62 (Jan. 19) 1924.

5. Busquet, H., and Vischniac, C.: Le poumon, organe de fixation elective de l'huile injectee dans le sang, Compt. rend. Soc. de biol. **84**:84 (March 14) 1921.

6. Warren, S., and Root, H. F.: Lipoid-Containing Cells in the Spleen in Diabetes with Lipemia, Am. J. Path. **2**:69 (Jan.) 1926.

lung, a certain amount of fatty material may be demonstrated histologically, but the amount is far less than that found in the cases here reported, and the droplets are always small. By way of a control, sections from twelve lungs showing extensive pneumonia in various stages of chronicity (some showing organization of the exudate) have been stained with scharlach R, and in no case has a picture been encountered which is at all comparable to that in the instances here reported. Furthermore, in pneumonic lungs the fat is found chiefly in the exudate, while in several of the cases here reported it was noted that the bronchioles, which contained more exudate than the alveoli, were strikingly free from oil or fat droplets. This is possibly because oil is removed from them by ciliary action.

A comparatively rare condition has been described,[7] in which large foam cells containing fat droplets are found in the alveoli of the lung, as well as in the spleen, thymus and other organs. It has been thought that these cells are "Kupffer" cells, which have been carried to the lung from the liver. These patients have a normal blood cholesterol and fatty acid content. They always show splenomegaly, and have been confused with Gaucher's disease. The cases reported here have no points of similarity with this group of cases.

It has been shown in the foregoing that a positive history of the use of fairly large quantities of some fatty or oily substance has been obtained in all six of the cases reported, and it will be shown later that the staining reactions, solubility, refraction, etc., of the material in the lungs were consistent with those of the particular material or materials administered in each case, as may be seen in the table. Moreover, the staining reactions, solubility and refraction were never completely consistent with those of neutral fats, cholesterin esters, fatty acids, soaps, phosphatids or cerebrosids (materials of a fatty nature ordinarily encountered under normal and pathologic conditions). These facts, together with the nature of the reaction on the part of the lung, all seem to substantiate the exogenous origin of the material much better than its endogenous origin.

### THE NATURE OF THE MATERIAL

Unfortunately, it was in most cases impossible to determine with any degree of certainty the exact nature of the oily substance in each case. In case 2, however, by utilizing a specific color reaction,[8] the material was determined almost beyond question to be cod liver oil.

This color reaction was obtained in an entirely characteristic manner when applied to the oil recovered from the lung tissue in case 2. A

7. Bloom, W.: Splenomegaly (Type Gaucher) and Lipoid-Histiocytosis (Type Niemann), Am. J. Path. **1**:595 (Nov.) 1925.

8. See U. S. Pharmacopea, under Olive Oil.

faint violet color was obtained in case 5, but attempts to concentrate the solution did not result in a characteristic reaction. In cases 3 and 6, no color at all was obtained. In cases 1 and 4, an insufficient amount of material was available to perform the test. Of five control tests made in ordinary cases of bronchopneumonia, no color reaction was obtained in three, a pale brown color in one and a faint yellow color in one.

Although it is probably unsafe to place too much reliance on a color test, these results, together with the facts that the staining reactions, solubility, etc., are completely consistent with those of cod liver oil and that the only discoverable oily substance given to this infant was cod liver oil, are regarded as good evidence that this was the oil involved in this instance.

In the other cases, the exact nature of the oily substances is somewhat problematic, but more than a guess can usually be made.

In case 1, a local physician had prescribed nose drops (to be administered by the patient's mother), the nature of which was not disclosed. The staining reactions, solubility, etc., of the material in the lungs in this case are more consistent with those of liquid petrolatum than with those of any of the other commonly used oils, and it seems probable that this was the material involved in this case. (This statement is based principally on the complete failure of the oil to reduce osmic acid, and its insolubility in dilute or absolute alcohol.)

In case 3, the only positive observation in the history was that the infant had been fed by gavage constantly for a period of several weeks. The staining reactions in this case were perfectly consistent with those of milk fat. The finding of starch grains (often two or three to each high power field) in a frozen section of the lung from this case also strengthens the view that material intended as food reached the alveoli. for this infant was also fed cereal by gavage.

In case 4, the question is more difficult, owing to the fact that olive oil nose drops, cod liver oil (in quantities of 5 cc. or more daily) and large amounts of egg-yolk were administered. Furthermore, only part of the material in the lung stained with osmic acid, and the staining with nile blue varied from deep blue to pink. This was one of the three cases in which prolonged fixation in potassium dichromate rendered the material (or rather a part of the material) impervious to any of the ordinary fat solvents.[9] This was found experimentally to be a property of egg-yolk, cod liver oil, castor oil, and, to a certain extent, of olive oil, but not of milk fat or mineral oil. Consequently, since egg-yolk is the only one of the substances tested which stained bluish with nile blue,

9. Ciaccio's method in Mallory and Wright: Pathological Technique, ed. 8, revised, Philadelphia, W. B. Saunders Company, 1924.

it seems most probable that egg-yolk and at least one of the other two oils were present in this instance. It is of interest to note that the property of thus being rendered insoluble by potassium dichromate is a property of certain fatty substances, especially the phosphatids. Egg-yolk contains a certain amount of lecithin, but cod liver oil and castor oil apparently contain no phosphatids.

In case 5 also, the question is complicated by a history of the routine use of cod liver oil, the administration of 4 cc. of liquid petrolatum daily for several weeks, and by gavage feeding. The fact that part of the material was absolutely unstained after prolonged exposure to osmic acid, stained pink with nile blue, and was not dissolved from frozen sections on formaldehyde-fixed material by absolute alcohol, seems to indicate that mineral oil was one factor in this case. About one half of the material stained deep brown with osmic acid, and was rendered insoluble in xylol and chloroform by fixation in potassium dichromate. This was presumably cod liver oil.

In case 6, it is clear, from the extreme degree of fibrosis, that the entrance of the oil into the lung must be sought many months before the child's death. A definite history of mineral oil by mouth and into the nares at various times during his life was obtained. The staining reactions point to the fact that only one kind of oily substance is involved in this case, and they are consistent with those of mineral oil only.

Summing up these conclusions, the material was probably mineral oil alone in two cases (cases 1 and 6), milk fat in one case (case 3), principally egg-yolk in one case (case 4), mineral oil and cod liver oil in one case (case 5), and cod liver oil alone in one case (case 2).

### MODES OF ENTRY

It seems difficult to believe that the small amount of cod liver oil given in a routine manner could find its way into the alveoli, but it is to be noted that in case 2 the infant had been given half an ounce daily.

Laughlin [3] has shown experimentally that in rabbits mineral oil given by mouth often enters the trachea, without any attempt to make it do so. (Its detection in the lung was insured by coloring it with scharlach R before administration.)

There are several considerations which make this occurrence seem probable in infants. In the first place, infants given an unwelcome substance such as cod liver or castor oil probably make no conscious effort to swallow it. When the act of swallowing is voluntary, there is little chance of false deglutition, because of the automatic closure of the trachea by the epiglottis. Assuming that the epiglottis did not function in this way, the trachea and esophagus would offer equally possible routes for a liquid running down into the larynx. In the second place, oil, being a bland substance, and being of such consistency that it moves

*Staining Reactions of Oily Material in Lungs*

| Case No. or Oil | Osmic Acid | Scharlach R | Nile Blue | Ciaccio's Method | Refraction | Solubility | Fat or Oil Used |
|---|---|---|---|---|---|---|---|
| 1..... | Negative | Orange-red | Light salmon | Negative | Negative | Insoluble in absolute alcohol; soluble in xylol and chloroform | Nose drops, nature unknown |
| 2..... | Dark brown | Orange-red | Pale salmon | Orange-yellow | Negative | Insoluble in absolute alcohol; soluble in xylol and chloroform | Cod liver oil |
| 3..... | Brown | Orange | Mostly salmon; few small blue droplets | Negative | Negative | Soluble in absolute alcohol, xylol and chloroform | Milk by gavage |
| 4..... | Part black; part brown | Orange-red | Mostly deep blue; part light pink | Orange-yellow | Negative | Zenker material insoluble in alcohol, xylol or chloroform | Cod liver oil; olive oil nose drops; egg yolk |
| 5..... | Half unstained (larger drops); half deep brown | Orange-red | Pink to salmon | Partly fixed; yellow | Negative | Insoluble in absolute alcohol; soluble in xylol and chloroform | Cod liver oil; mineral oil; milk by gavage |
| 6..... | Negative | Orange-red | Light pink | Negative | Negative | Insoluble in absolute alcohol; soluble in xylol and chloroform | Liquid petrolatum nose drops; paraffin oil by mouth |
| Olive oil..... | Brown | Red | Light pink | Orange-yellow | Negative | Slightly soluble in alcohol; soluble in xylol and chloroform | |
| Castor oil... | Brown | Red | Magenta | Orange | Negative | Soluble in absolute alcohol, xylol and chloroform | |
| Cod liver oil | Brown | Orange-red | Salmon | Orange | Negative | Slightly soluble in alcohol; soluble in xylol and chloroform | |
| Butter fat.. | Brown | Orange-red | Pink | Negative | Negative | Soluble in alcohol, xylol and chloroform | |
| Egg yolk.... | Brown | Orange-red | Blue-violet | Orange | Negative | Soluble in alcohol, xylol and chloroform | |
| Mineral oil.. | Negative | Orange-red | Pink | Negative | Negative | Insoluble in absolute alchohol; soluble in xylol and chloroform | |

slowly along the laryngeal wall, probably produces little sensation, and hence does not have as great a tendency to provoke a reflex closure of the epiglottis as do other liquid and solid substances.

Regarding the possibility of milk and other fatty foods reaching the lung, there is always the possibility of false passage of a gavage tube. (This is largely obviated if the tube is passed through the nares, for in this case it tends to hold its course more posteriorly.) The entrance of a gavage tube into the trachea is, as a rule, made at once manifest by the coughing and gagging of the patient, but there are, theoretically at least, other dangers from this method of feeding. If the liquid were given rapidly, and the cardiac orifice, because of temporary spasm or for other reasons, were unable to admit it to the stomach with sufficient rapidity, the fluid would rise in the esophagus until it reached the level of the tracheal opening, and if the epiglottis, because of the presence of the tube or because of the initiation of the act of coughing, did not at once close, the fluid might spill over into the trachea.

Allowing an infant to nurse from a bottle while lying on its back possibly increases the chances of false deglutition, and the administration of food during a comatose state is probably also a factor. (Aspiration of the stomach contents by regurgitation or vomiting is not an uncommon terminal event.)

### PATHOLOGIC SEQUENCES

It will be seen from the foregoing descriptions that this series of necropsies is a fortunate one for the study of the course of events following the arrival of the oil in the alveoli. The cases range from one which shows the earliest reaction (large oil-laden mononuclears in the alveoli only) to one which shows such marked nodular fibrosis that the condition was, on gross examination, suggestive of tumor formation. The duration probably varies from a few days to at least several months.

When oil enters the trachea, its progress downward is considerably resisted by the action of cilia possessed by the cuboidal epithelium of the trachea, bronchi and most of the bronchioles. One would suppose that a considerable amount of material must enter a bronchus in order that the effect of gravity should be sufficient to overcome this action of the cilia. Once having reached the alveoli, however, there is probably little tendency for the material to be expectorated.

The reaction to the oil in the alveoli is initiated by the appearance there of large numbers of large mononuclear phagocytes which engulf the smaller oil droplets, and often (in four of the six instances mentioned before) form multinucleated giant cells around the larger masses. The origin of these cells, which are identical with the "dust phagocytes," and probably also with the "epithelioid cells" in tuberculosis, has been a matter of great interest and dispute. The earlier view, that they are

modified epithelial cells, originating from the alveolar epithelium, has to a large extent been superseded by the belief that they are of endothelial origin. For an excellent discussion of this question, the reader is referred to a paper by Drinker.[10] In several of the cases here reported, it was noted that in those portions of the lung in which the fat was present in the alveoli and alveolar walls, the alveoli were uniformly lined with cuboidal epithelium, while in the uninvolved portions of the lung, the alveolar epithelium was composed of the normal platelike structures. In case 3, there appeared also to be considerable desquamation of these epithelial cells. Guieysse-Pellissier,[1] in studying the reaction in the lungs to olive oil introduced through the trachea, also noted that the alveolar epithelium became cuboidal, and thought that these epithelial cells "voraciously" engorged themselves with oil. In the cases here reported, the endothelium of the capillaries and more noticeably of the lymphatic vessels, showed marked proliferation, forming in many instances complete rings of endothelial cells about the oil drops, and sometimes even showing the formation of giant cells "in situ." Oil-laden cells were often seen lying in contact with the epithelium, but the fixed epithelial cells were always free from oil. These observations all appear to support the endothelial origin of the phagocytic cells, and it is thought that the resumption of the cuboidal type of epithelium by the alveolar walls is purely an incidental phenomenon, dependent on the atelectatic state brought about by the presence of the oil. Such an appearance is often noted in lungs which are atelectatic from other causes.

The reaction on the part of the lung to such oily substances furnishes an extremely favorable field for the further study of this question of the origin of the alveolar phagocytes.

The phagocytic cells, attracted to the oil globules by chemotaxis (?), probably reach the alveoli by passing between the epithelial cells lining the alveoli. Having acquired their load of oil, they again pass through the alveolar walls, and for the most part enter the lymphatics, which begin around the alveolar ducts and bronchioles. It has been shown in case 6 that some of the oil was deposited in the spleen. This could be explained by assuming that some of the oil-laden cells entered the alveolar wall capillaries directly, or that not all of the cells were held up in the bronchial lymph nodes, and a few of them reached the general circulation through the larger lymph channels.

In cases 2, 3, 4 and 5, the distention of the alveolar walls by this oily material in the lymphatics is obvious. Not all of the oil here appears to be situated intracellularly, and it is probable that at times cells containing more than they can hold either rupture and extrude

10. Drinker, C. K.: Modern Views on the Development of Lung Fibrosis, J. Indust. Hyg. **3**:295 (Feb.) 1922. (See attached bibliography.)

their material, or become necrotic and thus set it free. This in turn leads to further endothelial proliferation on the part of the lymphatics in which this happens. The large masses seen in some of the lymph channels are probably formed by coalescence of many smaller droplets.

This blocking and distention of the lymphatics causes a serious disturbance in the circulation through the lung, with consequent malnutrition of the tissues, and connective tissue formation begins, probably partly for the same reason that it occasionally does in severe chronic passive congestion, but largely as an attempt to wall off the globules of foreign material.

Eventually, a considerable amount of this material reaches the bronchial lymph nodes, where it is found in large quantities in case 6, but here, for some reason, it produces little fibrosis.

It is a matter of some interest that, in passing along the lymphatics, there may be extensive production of new lymph follicles (case 5) en route. This appearance is especially striking around the blood vessels and in the walls of the bronchioles (where lymph channels are most numerous). Similar appearances have been described in pneumokoniosis.[11]

The rate of flow through the lymph channels is probably fairly rapid at first, but, as the lymphatics become blocked, decreases, and may (case 6) nearly cease.

As has been brought out by Laughlin,[3] the carrying of bacteria from the nasopharynx into the alveoli probably plays an important part in causing the pneumonia which is a frequent concomitant of the reaction of the oil "per se." One might contend that the infectious process thus instigated was partly responsible for the fibrosis eventually resulting, but it is thought that in the foregoing cases the reaction to the oil can be separated from the reaction to the bacteria. The exact frequency of a complicating infectious process in this condition cannot be stated in this report, owing to the fact that cultural studies were not made of the lungs. In case 6, a careful study of many sections stained by Giemsa's method did not reveal any definite organisms. In case 3, streptococci were found in some of the bronchioles and a few of the surrounding alveoli, but organisms were nearly always absent from the alveoli, in spite of the fact that they contained many polymorphonuclears. In case 2, clumps of bacteria were found in the alveoli. In this connection it is of interest that Heiman and Aschner [12] have reported that the insufflation (intratracheally) of zinc stearate powder in dogs induced a type of aseptic

11. Irvine, L. G., and Watt, A. H.: Miners' Phthisis, Transvaal M. J. (now M. J. South Africa) **8**:30, 1912-1913. (Referred to by Drinker, footnote 10, reference not available.)

12. Heiman, H., and Aschner, P. W.: The Aspiration of Zinc Stearate in Infancy, Am. J. Dis. Child. **23**:503 (June) 1922.

interstitial pneumonitis. Wollstein and Meltzer,[13] insufflating various chemical substances (aleuronat, starch, egg-yolk and lecithin), conclude that "the consolidations of the lung produced by chemical substances differ from infectious pulmonary inflammations only in their sterility."

Weidman and Jefferies [14] have well described the histopathology of tumors produced by the subcutaneous injection of liquid paraffin in monkeys. In those cases in which the oil had remained in the tissues for several months, the picture is strikingly similar to that in the lungs in case 6 of this series. The absence of fibrosis in the regional nodes, in spite of the presence there of the oil in large quantities, is commented on by these workers, and is corroborated in case 6 of this series. Many instances of similar tumor formation have been described in human beings, following the subcutaneous injection of camphor oil and other substances incorporated in mineral oil. Because of the fibrosis and giant cell reaction, these tumors have often been mistaken for tuberculosis. Mook and Wander [15] describe six such cases, and observe that in the region of granulation tissue formation the subcutaneous elastic tissue is completely destroyed. This is in harmony with the observation in case 6 that the elastic tissue had disappeared from the alveolar walls in the areas of nodular fibrosis.

### ABSORPTION OF VEGETABLE AND ANIMAL OILS

It is of considerable importance to determine whether it is mineral oil alone which leads to this process of fibrosis within the body, or whether the digestible oils of vegetable and animal origin show a similar lack of absorbability. Weidman and Jefferies [14] conclude that olive oil and cottonseed oil are innocuous when injected subcutaneously, but admit that their position is somewhat insecure on this point. Sutton [16] has reported a case in which multiple tumors developed on the buttocks following the injection of mercurial salicylate in linseed oil. More significant are the experiments of Burrows and Johnston [17] on the subcutaneous injection of a brand of corn oil (mazola). These experiments were undertaken for another purpose, but incidentally they seem to show quite clearly that, as a rule, a vegetable oil of this nature is not absorbed under these conditions. Binet [18] has investigated the absorption of vari-

13. Wollstein, M., and Meltzer, S. J.: Experimental Chemical Pneumonia, J. Exper. Med. **28**:547 (Nov.) 1918.

14. Weidman, F. D., and Jefferies, M. S.: Experimental Production of Paraffin Oil Tumors in Monkeys, Arch. Dermat. & Syph. **7**:209 (Feb.) 1923.

15. Mook, W. H., and Wander, W. G.: Camphor Oil Tumors, Arch. Dermat. & Syph. **1**:304 (March) 1920.

16. Sutton, I. C.: Tumor Formation After Injection of Mercuric Salicylate in Vegetable Oil, Arch. Dermat. & Syph. **7**:223 (Feb.) 1923.

17. Burrows, M. T., and Johnston, C. G.: Action of Oils in Production of Tumors, Arch. Int. Med. **36**:293 (Sept.) 1925.

18. Binet, Leon: Physiologic Researches on the Resorption of Oil Injected Subcutaneously, Paris Letter, J. A. M. A. **86**:49 (Jan. 3) 1926.

ous oils injected subcutaneously. He finds that vegetable oils (such as olive oil) are absorbed slowly under these conditions, while certain animal oils are absorbed more rapidly.

It has been stated that the material in the lungs of three of the cases before reported stained black or brown with osmic acid. This fact, together with the other evidence, shows clearly that nonmineral oils were present. In cases 4 and 5, osmic acid reducing droplets were taken up by giant cells, and in both cases fibrosis had begun. This would seem to indicate that the absorption of nonmineral oils from the alveoli is a slow process at best.

The work done by Corper and Freed [2] was considered by them to throw some doubt on the advisability of injections of intratracheal oil for therapeutic purposes. Extensive use of this procedure for roentgenologic purposes is generally believed to have shown that it is practically without danger. It has been stated, however,[19] that in several instances a large part of the injected oil was still visible (by roentgen ray) in the lungs, three or four months after its introduction. In view of the facts brought out in the foregoing, it is difficult to believe that the use of such substances as iodized oil, 40 per cent, and iodipin intratracheally is entirely without harmful potentialities. This question should be answered by careful and thorough experimental work on animals.

## CLINICAL DIAGNOSIS

It might conceivably be possible to diagnose the condition described above by the finding of oil-laden phagocytes in the sputum. This has not been tried. There seems to be nothing in the symptomatology of the condition to distinguish it from ordinary bronchopneumonia, unless it be the lack of a rise in temperature, which was a rather striking feature in cases 3 and 4. The roentgenogram likewise shows nothing characteristic. The importance of diagnosing the condition is not great, owing to the fact that the treatment does not differ from that of simple pneumonia. The point of practical importance is that if the condition proves to be as frequent as this study would seem to indicate, it might seem wise to alter the method of administering oily substances to infants by mouth (as by incorporating them in their feedings), possibly by using nose drops in smaller quantities, and to feed by gavage only with the greatest caution against errors in technic.

## CONCLUSIONS

Six instances of oil aspiration in infants are reported, and conclusions have been drawn regarding the pathologic sequences.

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19. Iglauer, Samuel: Use of Injected Iodized Oil in Roentgen-Ray Diagnosis, J. A. M. A. **86**:1879-1884 (June 19) 1926. (Note especially discussion by Drs. Bronfin and Carmody.)

Oily and fatty substances given to infants by mouth and into the nasopharynx, as food or for purposes of medication, reach the alveoli of the lungs in many instances.

The oily or fatty droplets are taken up in the alveoli by large mononuclear phagocytes (probably of endothelial origin) and transported via the lymphatics to the tracheobronchial lymph nodes. A small amount of the material may get into the general circulation, and be deposited in the spleen.

The removal of this material from the alveoli, whether it be mineral oil or oils of vegetable or animal origin, is a comparatively slow process.

The end-result of such a process is similar to the reaction to any other foreign insoluble substance, namely, giant cell formation and fibrosis.

An acute infectious pneumonic process is usually superimposed on the picture described in the foregoing, and is probably the immediate cause of death in most cases.

Further clinical and pathologic observations and experimental work are needed to determine the frequency and importance of the condition here described, but this study seems to indicate that it is not a negligible factor in infant mortality.

# CONGENITAL DEFECT IN THE MUSCULATURE OF THE ABDOMINAL WALL

## REPORT OF A CASE *

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AND
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Congenital defect or absence of the musculature of the abdominal wall is a rare condition, but interesting in that postmortem examinations in these cases have revealed abnormalities of the genito-urinary system. In 1903, Stumme [1] compiled the cases recorded; in 1905 Garrod and Davies [2] collected all the cases published and added two of their own. In 1909, Mollison [3] arranged all cases reported, twelve altogether, in chronological order. He also added one case which he had under observation at that time. In 1913, Thatcher [4] next reported a case of congenital defect of the abdominal muscles with anomaly of the urinary apparatus, and the same year Smith [5] also presented a typical case in which a moderate degree of genu valgum and talipes calcaneovalgus were present on both sides. To this group of fifteen cases we add another in which the patient was admitted to the pediatric ward of the Minneapolis General Hospital.

### REPORT OF CASE

*History.*—R. T., a boy, aged 5 months, was the second child of healthy young parents. He was born at full term; the delivery was normal and no forceps were used. At birth, the obstetrician had made a note that the infant's abdomen lacked tone, but that the child nursed well and gained in weight satisfactorily. At the age of 2 months, the mother brought the infant back to the hospital dispensary. She then stated that she had no difficulty in nursing the child, but that she was much worried with regard to the child's abdomen which was large, soft and flabby. The use of a binder was advised, but several weeks later the mother returned to the dispensary much worried with regard to the thorax of the child, for the

* Received for publication, Oct. 12, 1926.

* From the pathological laboratory and the pediatric service (Dr. E. J. H. Huenekens, chief) of the Minneapolis General Hospital and the department of pediatrics, University of Minnesota.

1. Stumme, E. G.: Uber die symmetrischen kongenitalen Bauchmuskeldefekte und über die Kombination derselben mit anderen Bildungsanomalien des Rumpfes, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **6**:548, 1903.

2. Garrod, A. E., and Davies, W.: Group of Associated Congenital Malformations, Tr. Medico-Chir. Soc. **88**:363, 1905.

3. Mollison, W. M.: A Case of Congenital Defect in the Musculature of the Abdominal Wall, Guy's Hosp. Rep. **63**:23-28, 1909.

4. Thatcher, L.: A Case of Congenital Defect of Abdominal Muscles with Anomaly of Urinary Apparatus, Edinburgh M. J., n. s. **11**:127-134, 1913.

5. Smith, E. B.: Congenital Absence of Abdominal Muscles and Other Defects, Proc. Roy. Soc. Med. (part 1) **6**:186, 1912-1913.

sternum now protruded. It was tilted forward and upward, due undoubtedly to the lack of anchorage by the recti and other abdominal muscles. The child was then admitted to the hospital, for observation on March 23, 1926.

*Physical Examination.*—On admission, examination revealed a well nourished white boy, aged 5 months. The head and neck were normal, the thorax was deformed in that the sternum protruded toward the horizontal, but the muscles of the back and the pectoral muscles were well developed. The abdomen was large, flabby and bulged in the flanks (fig. 1). There were a number of deep

Fig. 1.—Appearance of the abdominal wall showing longitudinal furrows, leather-like wrinklings and a small slit-like umbilicus, simulating that of our own case, taken from Garrod and Davies.

longitudinal furrows. The umbilicus was represented by a linear scar about 1 cm. in length. There were numerous small horizontal furrows in the flanks. On palpation, no resistance was met, even when the child cried. Coils of the intestine could be felt; the liver and the spleen were easily palpable, the kidneys were palpable, and when full the bladder could be mapped out clearly. The testicles were undescended. The extremities were all well developed, no evidence

of any deformity being present. Repeated laboratory examinations revealed a normal urine, a normal blood picture, a negative Wassermann reaction and normal stools. A roentgenogram of the chest was negative.

*Course of Illness.*—The infant nursed satisfactorily and gained rapidly in weight the first week in the hospital, but on the tenth day he developed acute rhinitis and pharyngitis. The temperature rose from normal to 103 F., returned to normal on the thirteenth day, but again rose to 102 F. on the fourteenth day and then remained around 101 F. until death on the sixteenth day. Examination of the chest revealed evidence of pathologic changes at the base of both lungs close to the spine. Roentgenograms showed a shadow behind the heart suggesting pneumonia of the hilum. At the time of death, pneumonic signs were most marked in the lower left side of the chest.

*Necropsy (Partial, Through a Small Abdominal Incision).*—The body was embalmed. It was well developed, except for the abdominal wall, and fairly well nourished, weighing about 15 pounds (6.8 Kg.). The skin showed marked pallor. The abdominal wall was greatly relaxed, thin and protruded like a leather bag. It showed longitudinal striations and was wrinkled in the flanks. It was disproportioned, the right half being more prominently distended due to accumulation of the loops of the intestine on this side of the abdominal cavity. The umbilicus was small, and was represented by a narrow longitudinal slit surrounded by a narrow zone of wrinkles.

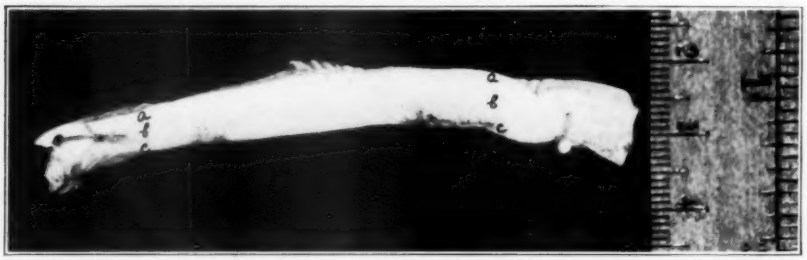


Fig. 2.—Cross-section of the abdominal wall at the median line, showing (*a*) the skin, (*b*) the thick fat layer and (*c*) the transversalis fascia.

The subcutaneous adipose tissue of the abdominal wall was white and dense, being 7 mm. in thickness in the median line. It rested immediately over the transversalis fascia, there being no gross evidence of abdominal musculature throughout the entire abdominal wall. Here the abdominal wall was 9 mm. in thickness (fig. 2). The adipose tissue in the flanks was 5 mm. thick. A dense fibrous band bound the umbilicus to the urinary bladder anteriorly. Most of the bladder was located slightly to the left of the median line and was considerably raised above the symphysis pubis. The appendix hung free.

The heart appeared normal on gross inspection. The left lung showed a massive consolidation of the lower lobe, the cut surfaces being grayish red and homogeneous, with droplets of pus exuding on pressure. The right lung revealed impaired crepitation throughout the lower lobe. The cut surfaces were edematous and hemorrhagic.

The spleen, liver and gastro-intestinal tract were normal. The left kidney weighed 10 Gm.; the capsule stripped readily, leaving a smooth, rounded surface. The cut surfaces showed no gross abnormality. The right kidney weighed 35 Gm. The capsule stripped readily, leaving a smooth lobulated surface. The cut surface showed normal markings. The ureters were small, the wall being thick and the lumen narrow. The bladder (fig. 3) was greatly enlarged, measuring 6.5 cm. in length, 4.5 cm. in width and 2.5 cm. anteroposteriorly. The bladder wall was contracted and diffusely thickened, measuring 1 cm. in thickness at the dome which was smooth and rounded and was located just left of the median line. The trigone

and ureteral openings appeared normal. The ureters were not dilated. The urachus was densely fibrotic, and revealed no patent lumen. The testes were not present in the scrotal sac. They were also absent in the inguinal canals and along the ureters. No further search for them was possible because of the short length of the incision. The diaphragm was thickened, the right side being 3 mm. in thickness; the left, 4 mm.

*Microscopic Examination.*—Sections from the midline of the abdomen showed a normal skin and its appendages, a wide zone of adipose tissue and only a few fragments of striated muscle fibers resting on a definite transversalis fascia (figs. 4 and 5). Sections from the lateral part of the abdomen revealed some evidence of definite fascial planes, but no evidence of muscle tissue. The con-

Fig. 3.—The bladder, showing (*a*) the enormous hypertrophy of the wall.

solidated area of the lower lobe of the left lung showed desquamation of the epithelium of the bronchi which were also filled with pus cells. The alveoli about the bronchi were filled with pus cells in patches and a few desquamated alveolar cells. The alveolar capillaries were dilated; the whole picture was that of a confluent bronchopneumonia.

The spleen showed slight congestion throughout, while the liver showed slight congestion beneath the capsule. The section of the left kidney revealed much fibrosis particularly around the pelvis; the right kidney was normal. The bladder showed a marked increase of the fibrous tissue of the wall between the bundles of the muscle tissue which was also increased (fig. 6). Sections of the diaphragm showed that most of the muscle fibers were at least of normal size and the remainder were slightly hypertrophied.

COMMENT

With regard to the relationship of the changes in the genito-urinary system to the defect in the musculature of the abdominal wall, Guthrie,[6] in 1896, stated that the muscular deficiency of the abdominal wall and the high position of the bladder are dependent on the failure of development during the intra-uterine life, the hypertrophy of the bladder being a secondary condition. In his case, the bladder, being firmly connected with the umbilical scar, was unable to contract downward and empty itself completely. As a consequence, it became hypertrophied

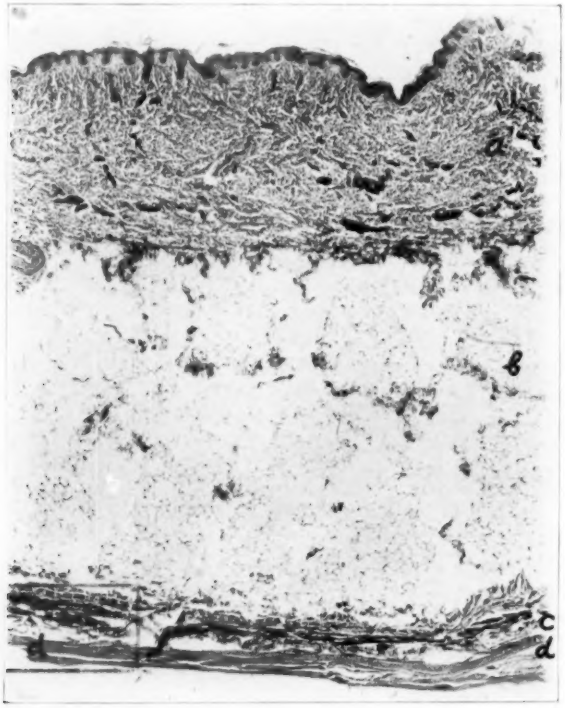


Fig. 4.—Microscopic section of the abdominal wall (fig. 2) showing (*a*) the skin and the appendages, (*b*) the adipose tissue, (*c*) fragments of the muscle fibers and (*d*) the transversalis fascia.

and dilated. The urinary accumulation caused a backward pressure in the ureters, which became dilated. In 1901, Osler[7] had a case; he referred the problem to Dr. Bardeen who suggested two possible explanations, which are as follows:

6. Guthrie, L.: Case of Congenital Deficiency of the Abdominal Muscles, Tr. Path. Soc. London **47**:139, 1896.

7. Osler, W.: Congenital Absence of the Abdominal Muscles with Distended and Hypertrophied Urinary Bladder, Bull. Johns Hopkins Hosp. **12**:331, 1901.

1. It is possible that the lack of resistance normally met with in the abdominal wall by the bladder, at the time when the kidneys began to secrete urine, may cause the bladder to expand rather than to empty secretions into the amniotic cavity through the urethra.

2. Under normal conditions the growth of the abdominal musculature is preceded by the formation of a vascular plexus, supplied ffrom above from the internal mammary, from below by the epigastric artery. It is possible that an abnormal arrangement of the blood vessels in the embryo prevented the formation of this plexus, and impeded the growth of the abdominal musculature, and that, at the same time, these circulatory disturbances also gave rise to the abnormal conditions found in the bladder and ureters.

Fig. 5.—High power magnification, showing (*a*) the muscle fibers and (*b*) the transversalis fascia.

Thus two possibilities are here presented, first, that the bladder condition is secondary to the musculature defect, and second, that both conditions arise from the same cause. Stumme, however, in 1903 offered a third possible explanation. He stated that late in the embryonic life an occlusion of the urethra occurred causing retention of urine, to which the bladder and ureters responded by hypertrophy and dilatation. Through the pressure of the much dilated bladder and possibly of the ureters also, atrophy of the greater part of the abdominal musculature was brought about. The enlargement of the bladder also interfered with the return of blood from the embryo, causing possibly the development

of ascites, which further increased abdominal distention. Finally, the large bladder hindered the entry of the testicles into the processus vaginalis and their descent into the scrotum. Later, Stumme stated that the cause of the retention of urine disappeared. The abdominal walls contracted and became thrown into folds; the bladder also shrank but was unable to sink down into the lesser pelvic cavity.

Garrod and Davies accepted the view that the condition of the abdominal musculature was secondary to dilatation of the bladder. They consider the fact that the abdomen showed evidence of having

Fig. 6.—Microscopic section of the bladder wall showing a dense fibrosis.

been greatly distended by pressure within, and this distention had already disappeared at birth, for at that time the abdomen was peculiarly flattened. Then, too, the absence of muscle tissue was most marked in the central and anterior portions of the abdominal musculature, there being, in many cases reviewed by these authors, comparatively well developed muscle tissue near the peripheral attachment of the abdominal muscles. Such a condition was just what they expected on account of the pressure within, as by a distended bladder. Dr. Batten, who examined microscopic sections from one of their patients, considered that the rudiments of muscle tissue in the abdominal wall

suggested a failure of development rather than atrophy. No explanation is given for the temporary obstruction of the urethra during intra-uterine life, which Stumme's theory involves.

Mollison stated that his case could not be explained by the theory of Garrod and Davies. His case did not bear out this theory because the bladder was not abdominal in position, and there was no indication of enlargement of the ureters. He divided all cases into two groups. In the first group he placed all patients who died before the age of 1 year. All of these children had some anomaly or abnormal condition of the urinary tract. In the second group were all those who survived for at least two years. In these children the lack of development of the abdominal muscles with partial absence might account for the hypertrophy of the bladder and the dilatation of the ureters later. Mollison's patient was 3 years old, and there was no evidence of the hypertrophy of the bladder or the dilatation of the ureters, but he stated that possibly at some future time the bladder would hypertrophy and give rise to back pressure on the ureters and the kidneys.

With regard to our case, Prof. R. E. Scammon of the anatomy department believes that the abdominal condition is due simply to a failure or arrest of the embryonic skeletal muscle tissue to extend forward into the anterior body wall and therefore to develop into the abdominal musculature. What the etiologic factors are which prompt this failure or arrest in the course of otherwise normal development of the embryo, we are not prepared to answer in the present communication. We are of the opinion that in our patient at least the hypertrophy of the bladder is probably a secondary development.

## SUMMARY

1. A case of congenital defect in the anterior abdominal musculature with anomalies of the genito-urinary system is presented.

2. The condition was characterized grossly by a protruding sternum, a large, flabby, soft abdomen, a slitlike umbilicus and the undescended testes. At necropsy, the anterior abdominal wall showed a thick layer of adipose tissue but no muscles grossly demonstrable. The bladder was hypertrophied and the diaphragm was thickened. The kidneys were unequal in size. Microscopically, no musculature was found in the lateral aspects and only a few fragments of rudimentary muscle fibers in the anterior portion of the abdominal wall. The small kidney showed fibrosis about the pelvis. The bladder showed a marked increase in fibrous tissue. The bladder and the diaphragm showed hypertrophy of the muscle tissue.

3. The literature is reviewed and discussed. Special emphasis is placed on the theories of Stumme and of Garrod and Davies as to the etiology of the conditions found in our case.

# PROGRESS IN PEDIATRICS

## THE EARLIEST REPORT OF CONGENITAL PYLORIC STENOSIS

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In 1902, Cautley and Dent stated that the earliest record of congenital pyloric stenosis was that of a case report dated 1841.[1]

William Osler took exception to this statement,[2] and, in 1903, set forth the claims of Hezekiah Beardsley,[3] whose monograph, "A Case of Scirrus in the Pylorus of an Infant," he had found in the course of a study that he was making in early American medical literature.

In 1918, I reported that a true case of this disease, occurring at the third week of life, had been described by George Armstrong, in 1777, antedating the report of Beardsley by eleven years.[4]

It happened that, in 1917, while reading some eighteenth century English texts on pediatrics, through the kindness of Lieut. Col. Fielding Garrison, in the Surgeon General's Library, I came across two works by George Armstrong, a London physician, who lived in the latter part of the eighteenth century. The earlier work was entitled "An Essay on the Diseases Most Fatal to Infants." This was first published in 1767, and a new edition issued in 1771. The 1771 edition was not in the library, being at that time in the bindery. In 1777, another work by Armstrong appeared, entitled "An Account of the Diseases Most Incident to Children from Their Birth to Puberty."

In comparing these two publications, I found that the second was an amplification of the first, with the title changed. On page 49 of the first edition of the "Account of the Diseases Most Incident to Children," published in 1777, Armstrong reported that a child, aged 3 weeks, had died, and an autopsy had revealed a hard and contracted pylorus. The child, he concluded, had died of a spasm in the pylorus. He described a typical clinical course and the usual pathologic condition of congenital pyloric stenosis. Besides priority of publication of his article by eleven years, Armstrong described a typical case of the disease, while in Beardsley's case, because of the age of the patient (5 years) and the concomitant pathologic changes in the gallbladder, the diagnosis was

1. Cautley and Dent: Lancet, Dec. 20, 1902.
2. Osler, William: Arch. Pediat., 1903, p. 355.
3. Beardsley, H., in Cases and Observations of the Medical Society of New Haven County, 1788, pp. 81-84.
4. Foote, John: Pylorospasm, Am. J. Dis. Child. **15**:351 (May) 1918.

presumptive rather than positive. On searching the literature, I could not find any evidence that attention had ever been called to this notable clinical discovery made by George Armstrong so long a time before other clinicians.

Since my publication of the report of this case in 1918, a number of authors have properly credited Armstrong with the first report of this condition, although many others still erroneously attribute priority to Beardsley's nontypical case. Another bibliographic error has arisen by the usage of some writers in quoting Armstrong's original publication (1767) as the source of the first case. This is obviously wrong, since reference to this case does not appear in the first edition in 1767 of the "Account of the Diseases Most Fatal to Infants." A copy of the second edition published in 1771 was not available at the time I made my report in 1918. However, a little later I obtained a copy of the 1771 edition and found in it the description of the case of pyloric stenosis, literally word for word, that I had quoted from the 1777 work, with a different title which had been published six years later.

This gives Armstrong's report a further priority over Beardsley's questionable case and makes his record seventeen years prior to that of the American author. In giving the source of the first description of this disease it is not correct, however, to report George Armstrong's description as having been published in "An Account of the Diseases Most Fatal to Infants, etc." in the edition of 1767, but it is correct to refer it to the second edition of 1771. It also appears in the volume from which my quotation was made, entitled "An Account of the Diseases Most Incident to Children, etc." (pp. 49-50) published in 1777 as well as in the later edition of 1783, and in the edition edited by Buchan which appeared in 1808. The date of first publication, therefore, should be given, not as 1767, which is too early, or as 1783, which is too late, but as 1771.

# CEREBRAL BIRTH PARALYSIS

## FACTORS WHICH INFLUENCE PROGNOSIS AND TREATMENT *

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ST. LOUIS

The wide variation in type of the motor disturbances seen in children with so-called cerebral birth paralysis has made a more accurate classification of these disorders extremely difficult. Knowledge of the cerebral functions is still incomplete, and opportunities for necropsies in cases which have been carefully studied clinically are relatively rare. Perhaps the most commonly reported pathologic lesions in this type of spastic paralysis are those involving gross defects of the cerebral cortex, often associated with lack of development or injury to the pyramidal tracts. In addition, recent research on the function of the corpus striatum makes it seem likely that some of the most bizarre of the motor disturbances may be explained by lesions in the region of the lenticular and caudate nuclei.[1]

The origin and nature of such lesions are frequently uncertain, although pediatricians are inclined to attribute a great many to intracranial hemorrhage occurring at or near the time of birth. This view, however, has lately been questioned seriously by certain neurologists.[2] Supporting the theory that intracranial hemorrhage is at least one of the most important factors are the numerous reports showing the frequency of such accidents in newly born infants, and the individual instances in which children with clinical evidence of intracranial hemorrhage at birth have later developed typical spastic paralysis. Additional evidence of great importance is supplied by the recent contributions of Philip Schwartz,[3] citing careful anatomic studies of the brains of more than 300 infants of various ages who had suffered cerebral injuries at birth.

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* Read before the meeting of the American Pediatric Society, Niagara Falls, Canada, June 2, 1926.

* From the Department of Pediatrics, Washington University School of Medicine, and the Shriners' Hospital for Crippled Children, St. Louis Unit.

1. Crothers, B.: Lesions of the Corpus Striatum in Childhood with a Report of Clinical Cases Illustrating Various Syndromes, Am. J. Dis. Child. **22**:145 (Aug.) 1921.

2. Collier, J. S.: Pathogenesis of Cerebral Diplegia, Proc. Roy. Soc. Med. (Sect. Neuro.) **17**:1 (Jan.) 1924; Brain **47**:1 (Feb.) 1924.

3. Schwartz, P.: Erkrankungen des Zentralnervensystems nach traumatischer Geburtschädigung, Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:263, 1924; Schwartz, P., and Fink, L.: Morphologie und Enstehung der geburtstraumatischer Blutungen im Gehirn und Schädel des Neugeborenen, Ztschr. f. Kinderh. **40**:427, 1926.

Brain injuries of this nature which are not promptly fatal are usually followed by the development of a spastic paralysis involving one or more extremities, and are often associated with more or less mental deficiency, incoordination or athetosis. Occasionally, despite a history of birth injury and delayed development, there may be absence of rigidity and spasticity, or even the presence of marked hypotonia with ataxia and increased mobility of the joints. In any case the outlook is discouraging at best, for progress is slow and it is difficult to foretell the amount of improvement which may be expected from the various orthopedic measures usually employed. However, as a result of an unusual opportunity for studying a large number of children with spastic paralysis, the criticism seems justified that the presence of certain symptoms definitely influences the prognosis and may prove helpful in determining the proper treatment.

During the past two years, 238 children suffering from spastic paralysis were received for examination at the Shriners' Hospital in St. Louis. Of these, 159 were admitted to the hospital for operation and further study and seventy-nine were examined in the outpatient department. All patients were carefully examined by the pediatrician, neurologist, orthopedic surgeon, laryngologist and dentist. Those in the hospital in addition were tested by the routine Wassermann, Pirquet and Schick tests, a blood count was made, as were urinalysis and other routine tests. In general, it may be said that the most severe manifestations of the disease, with the least tendency toward improvement, were seen in the children with athetosis, ataxia or mental deficiency. In spastic paralysis then, these three symptoms usually denote a bad prognosis with regard to future improvement. Severe disability, which at first may appear to be the result of spasticity, on closer observation may prove to be due entirely to athetosis. On the other hand, ataxia without rigidity offers a relatively good prognosis except in those patients who give a history of progression of the disease. Even in children with extreme spasticity, there are usually periods of partial relaxation of the muscles and marked differences in the extent of the involvement of the two sides of the body. Moreover, the mentality is often surprisingly good, although the presence of a marked athetosis can make speech so difficult that the child appears to be mentally deficient.

Patients with all types of lesions except those obviously hopeless have been accepted for treatment, but the following criteria have been recognized as being most favorable for the best results: (1) the child must be of normal or nearly normal mentality; (2) he must give a history of improvement in his condition; (3) he must have no athetosis or marked incoordination of movements other than those due to the spasticity, and (4) he must be willing and old enough to cooperate in the postoperative exercises.

The treatment of spastic paralysis, regardless of etiology, consists of the employment of various orthopedic measures which have as their object the correction of deformity, the strengthening of weak muscles and reeducation of the patient in their use. In the mildest type of spastic paralysis, massage, active and passive corrective exercises and supervised training in walking, etc., may prove sufficient to cause marked improvement. In more severe types, however, some surgical interference is usually necessary to overcome the handicap of contractures or spastic muscles. For this purpose the operation most often performed is tenotomy of the affected muscles, followed by overcorrection of the deformity in a plaster cast.

In the series of cases at the Shriners' Hospital, however, much better results have followed the use of peripheral neurectomy. Resection of the sympathetic nerve (ramisection), as advocated by Royle [4] and Hunter,[5] was not attempted, because this operation was regarded as being still in the experimental stage.

I am indebted to Dr. LeRoy C. Abbott for the following brief résumé of the routine followed in the series of cases mentioned in the foregoing.

### ROUTINE METHOD OF TREATMENT

The case being selected as one suitable for operation, a careful study is made to determine which of the muscles are most spastic and whether such contractures as may exist are due to spasm or structural shortening of the muscles. Only the most severe contractures require myotomy, the other deformities being overcome by forced extension of the hip, or through stretching the hamstrings and Achilles tendon by wedging in plaster. In bad contractures, correction may be obtained only by fasciotomy at the hip, lengthening the heel cord, etc. It is important, however, that all corrective measures, except the operative ones, be carried out before neurectomy is attempted. Following this procedure in the lower extremity, resection of the nerve has been carried out on the obturator nerves, the sciatic branches to the hamstrings, and the popliteal branches to the gastrocnemius and soleus muscles.

In the arm, neurectomy has been performed on the median nerve branches to the superficial head of the pronator teres, as well as a partial division of the nerve supply to the flexors of the wrist and flexors of the fingers and thumb. In patients with marked spasm of the adductors, complete section of the obturator nerves is performed within the pelvis above the nerve branches, whereas in mild cases, division of the anterior branch in the groin may prove sufficient.

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4. Royle, N. D.: New Operative Treatment of Spastic Paralysis, M. J. Australia **1**:77 (Jan. 26) 1924.

5. Hunter, J. I.: Postural Influence of Sympathetic Innervation of Voluntary Muscle, M. J. Australia **1**:86 (Jan. 26) 1924.

Postoperative care and subsequent training are extremely important, and on these the success of the operation often depends. In all marked cases of spasticity of the muscles, the opposing muscle groups have usually been stretched, and as a result are very much weakened. The muscles of the leg in which such weakness most often occurs are the gluteals, the quadriceps and the dorsal flexors of the foot, and success in walking is often directly proportional to the strength developed in these muscles. Accordingly, following operation the limbs are placed in plaster fixation to prevent recurrence of the deformity and to maintain relaxation of the stretched muscles. Splints are removable to permit of passive, and later, active exercises of the atrophied muscles, efforts being made in this way to reestablish the balance between the opposing muscle groups. When the patient shows a return of power in these congenitally weak muscles, then and only then should he be permitted to walk, under skilled direction. It is exceedingly difficult to induce patients to stand erect even after all this treatment, for there is a tendency to return to the former attitude. In this connection, it has been found helpful to place the patient erect in a large tank of water in which he can not only exercise his muscles more freely, but also can gain a better sense of balance. Exercises in walking while supporting the arms by parallel bars, or the use of a large walker patterned after those made for infants, are also helpful in the early stages of training. To avoid resuming the old posture, the child may wear some removable apparatus to hold the knee in extension when first attempting to walk, and this may also be worn at night for an indefinite time. This skilled and painstaking after-care must, of course, be carried out for many months, but if faithfully adhered to, the improvement is usually extremely gratifying. Occasionally progress may be impeded by the presence of deformities of the feet, and in these, stabilization operations, such as the Hoke operation, may prove helpful. Similarly, additional power can often be supplied to the hand by means of an arthrodesis of the wrist joint.

SUMMARY

Two hundred and thirty-eight children with spastic paralysis were examined in consultation with a neurologist and orthopedist and the following symptoms, in the order of their importance, were found to indicate a relatively bad prognosis: (*a*) mental deficiency, (*b*) progression of the disease, (*c*) athetosis and (*d*) ataxia.

The most successful treatment was found to be peripheral neurectomy of the nerves of supply to the spastic muscles, followed by carefully supervised training which aims at restoring the proper balance between the opposed muscle groups.

# News and Comment

## UNITED STATES PUBLIC HEALTH SERVICE

The weekly Public Health Reports of the United States Public Health Service now are available to all persons in the United States and its possessions, and in Canada, Cuba and Mexico, for the nominal subscription of $1.50 per year, it was announced in the current issue of the official bulletin of the Post Office Department.

Subscriptions should be accompanied by money orders, and sent to the Superintendent of Documents, Government Printing Office, Washington, D. C.

## DEATH OF DR. ROLDAN

D. Jacobo Banqueri Roldan, physician at the Hospital del Nino Jesus, Madrid, a distinguished Spanish pediatrician, died recently.

## ANOTHER ROENTGEN-RAY VICTIM

Dr. Félix Lobligeois, for twenty years roentgenologist in the children's hospital, Bretonneau, Paris, is another victim of the roentgen rays. He lost the entire right arm following a series of partial amputations. The Croix d'Officier de la Légion d'Honneur and the Médaille de Fondation Bergonié have recently been conferred on him.

## NEW ITALIAN JOURNAL

A new bimonthly journal of pediatrics has appeared in Turin, Italy, under the name *Clinica ed Igiene infantile*. Prof. Enrico Mensi is the editor.

## CHILD MORTALITY IN INDO-CHINA

Measures taken for the reduction of child mortality in Saigon, the capital of French Indo-China, have met with remarkable success, according to *La Presse Médicale* for Dec. 1, 1926. In 1905, the infant mortality was 23.85 for each one hundred of the population; in 1925, it was 5.8. In the same period, the deaths of children under 6 years fell from about 40 to 12.93 per cent.

## CORRECTIONS

A printer's error occurred in the article by Dr. Weston A. Price, "Calcium Metabolism Studies," appearing in the January issue of the American Journal of Diseases of Children. The second sentence on page 91 should read: "Figure 8 *shows the teeth of a boy at 7 years of age* (A), and again at 11 (B), during which time the deciduous teeth had not been normally exfoliated or the permanent teeth erupted, which should have taken place at 9 or 10 years of age.

In the article by Dr. Frederic W. Schlutz, "Heliotherapy and Actinotherapy in Relation to Pediatrics," in the department of Progress in Pediatrics, in the January issue, an error in the spelling of Dr. Louis Fischer's name occurs on page 128, at the beginning of the last paragraph, and on 134, in the bibliography.

# Abstracts from Current Literature

## Anatomy and Physiology

Umbilical Cord. Norris W. Vaux and William Belk, J. A. M. A. **87**:154 (July 17) 1926.

A study of the umbilical cord revealed a surprising number of anatomic variations. The authors hope to be able to demonstrate that these anomalies are closely associated or in part may be the etiologic factor associated with some of the fetal deaths or accidents of intra-uterine life.

Bonar, Salt Lake City.

## Pathology, Bacteriology and Biochemistry

Blood Chemistry Changes in Children Produced by Exposure to the Alpine Lamp. E. M. Greisheimer and A. W. Arnold, Am. Rev. Tuberc. **14**:479 (Oct.) 1926.

Treatment with the Alpine lamp seemed not to have any effect on the blood calcium or the acid soluble phosphorus of the plasma in eight girls between the ages of 10 and 16 with masked juvenile tuberculosis. Eight boys were used as controls.

Smith, Ogden, Utah.

A Comparison of the Folin-Wu and the New Benedict Method for Sugar in Blood and Cerebrospinal Fluid. J. D. Lyttle and J. E. Hearn, J. Biol. Chem. **68**:751, 1926.

Simultaneous blood and cerebrospinal fluid determinations were made by the Folin-Wu and the new Benedict method. The Folin-Wu method gave generally higher values than the Benedict method, although there was less divergence in the spinal fluid than in the blood analyses. The difference in sugar content obtained by the two methods is not related to the protein or nonprotein nitrogen content of the spinal fluid nor to the nonprotein nitrogen content of the blood.

Arthur Locke.

A Study of the New Benedict Method for the Determination of Blood Sugar. R. Rockwood, J. Biol. Chem. **69**:187, 1926.

The new Benedict method for blood sugar was compared to the Folin-Wu method in a series of 300 samples of blood. The Benedict reagents which have been used to date do not require as great a correction for lack of proportion in color development as the Folin-Wu reagents. The normal cases in this group show a mode between from 75 to 85 mg. per hundred cubic centimeters and a range of from 50 to 120 mg. The difference value between the Folin-Wu and Benedict methods does not seem to be correlated with any factor in the condition of the diabetic patients. The cuprous oxide precipitate in the Benedict test is more difficultly soluble than in the Folin-Wu test, especially with high blood sugars. The substance causing the difference value is apparently not one of the ordinary nitrogenous reducing substances since the difference value is not increased in uremia. Sugar tolerance tests show no

characteristic variation in the difference value. The substance causing the difference value seems to be present in greater quantity in the cells than in the plasma and sometimes is present only there.

AUTHOR'S SUMMARY.

EFFECT OF THE AMINO ACIDS AND DIALYZABLE CONSTITUENTS OF EMBRYONIC TISSUE JUICE ON THE GROWTH OF FIBROBLASTS. LILLIAN E. BAKER and ALEXIS CARREL, J. Exper. Med. **44**:397, 1926.

The ultrafiltrable constituents of embryonic tissue extract are unable to support cell life in vitro. They stimulate cell migration and possibly multiplication, without increasing the mass of the tissue. Embryonic tissue extract freed from amino acids by dialysis still retains a considerable part of its growth-promoting properties. The area of growth of tissues in embryonic tissue extract free from amino acids is appreciably less than that with the whole extract, probably owing to the denaturation of part of the protein, or perhaps to the inactivation or loss of an enzyme. The addition of either the unfiltrable components or an artificial mixture of amino acids to this dialyzed extract increases the area of cell migration but does not restore all the activity lost on dialyses. The observed differences in growth of tissue, due to the addition or removal of dialyzable and ultrafiltrable constituents of the extract, prove that the amino acids produce a more active cell migration and possibly multiplication, but no building up of new protoplasm.

AUTHORS' SUMMARY.

THE FUNCTION OF A PHOSPHATASE IN BONE-FORMATION. H. D. KAY, Brit. J. Exper. Path. **7**:180, 1926.

In normal blood plasma a small quantity of an acid-soluble phosphoric ester is present which is hydrolyzable by bone phosphatase. This may be an important factor in bone formation and maintenance. The phosphatase content of the whole bone is extremely high in fetal life, but diminishes as the rate of bone formation decreases. In the whole kidney, the phosphatase is lowest in the fetal stage, and rapidly increases as the kidney becomes functional.

S. A. LEVINSON.

THE STUDY OF AGGLUTININS FOR THE ORGANISMS OF DYSENTERY. G. BARBERA, Clin. pediat. **8**:267 (May) 1926.

Besides its own specific receptors, the organism possesses other receptors for agglutinins of homologous bacteria. Preformed agglutinins do not exist in the blood serum, but they are produced each time bacteria enter the body and remain for an indefinite period. In his studies, the author observed agglutination rarely in young patients, and noted a proportionate increase in agglutinins with advancing age. If agglutination occurs in children and adults in good health, at a relatively low dilution, the reaction is of value only when the dilution is greater than 1:100.

STUDIES ON THE BLOOD CHEMISTRY OF INFANTS. G. DITONI, Clin. pediat. **8**:449 (Aug.) 1926.

The author reports an exhaustive study of the progress in blood chemistry and urges that its study be more widely adopted than it is at present, because of the fact that from a single specimen of blood a great deal of valuable information can be obtained regarding its organic and inorganic constituents.

He proposes a complete system of analysis which requires from 17 to 20 cc. of blood. The blood is rendered incoagulable by lithium citrate. The proteins are extracted partly by the method of Folin and Wu and partly by the method of Kramer and Tisdall. The estimation for cholesterol and lecithin are made on the protein residue. From the filtrate, determinations are made of the nonprotein nitrogen, urea, uric acid, creatinine, creatine, glucose and chlorides. From the filtrate, treated with trichloracetic acid, the quantities of sodium potassium, calcium, magnesium and phosphorus can be estimated.

ZAMBARANO, Northville, Mich.

STUDIES REGARDING BLOOD GROUPS IN INFANCY. FILIPPO FERRARO, Riv. di clin. pediat. **24**:758, 1926.

The author determined the blood group to which 131 infants belonged and found them distributed as follows: group I, 55, or 41.3 per cent; group II, 59, or 44.3 per cent; group III, 15, or 11.2 per cent; group IV, 4, or 3 per cent. The cells of group I were not agglutinated by any serum. The cells of group II were agglutinated by serums of groups I and III. The cells of group III were agglutinated by serums of groups I and II. The cells of group IV were agglutinated by serums of groups I, II and III.

This distribution is approximately the same as that reported by other investigators for both infants and adults.

The blood group of fifteen children, with various diseases such as diphtheria, typhoid fever, spasmophilia and syphilis, was unchanged as the result of treatment with diphtheria antitoxin, methenamine, ultraviolet irradiation, roentgen ray and mercurial injections.

The blood groups of nursing infants and their mothers were found to be the same in thirteen instances and different in thirteen instances. The mother's cells were agglutinated by the infant's serum in nine cases, and the infant's cells by the mother's serum in four of the twenty-six cases.

Observations were made as to the blood groups of six pairs of twins. In each case, one child was of the same blood group as its twin.

In fourteen cases, the blood group was determined both before and after death. No change was found in the grouping, even as long as forty-eight hours post mortem.

HIGGINS, Cincinnati.

THE EFFECT OF CERTAIN AMINO-ACIDS ON THE ACTION OF DIPHTHERIA TOXIN. B. SBARSKY and L. SUBKOWA, Biochem. Ztschr. **172**:40 (May) 1926.

The toxicity of diphtheria toxin for guinea-pigs is diminished by the simultaneous injection of certain amino-acids (tyrosin, glycocoll, alanin). The varying degree of adsorption of the toxin and the acids by the red cells is given as an explanation of the results. Tyrosin prevented death in some cases.

THE EFFECT OF VARIOUS VITAMIN CARRIERS ON THE PHOTOGRAPHIC PLATE. H. VOLLMER, Biochem. Ztschr. **172**:467 (May) 1926.

This is a preliminary report on the relation of antirachitic substances and their photo-activity. A great many vegetable and animal fats were tested before and after exposure to ultraviolet rays. Some (cod liver oil, olive oil, oil of turpentine) were photo-active before "raying," but almost all (except paraffin) were photo-active after exposure to ultraviolet rays. Some substances that were antirachitic after "raying" were not photo-active. These included milk, egg

yolk, fresh vegetables and the non-saponifiable part of cod liver oil. This may be explained by the presence of chromatin or of protein, which absorbs the energy of the rays.

The substances liberated iodine from a solution of potassium iodide in proportion to their photo-activity.

M. B. Brahdy, New York.

Further Investigations on the Buffer Reaction in Fever. Otto Beck, Jahrb. f. Kinderh. **113**:198, 1926.

In the examination of the urine in five cases of fever, three of which were due to vaccination and two to a combination of measles and vaccination, there was an increased output of ammonia which remained high until convalescence had set in. The amount of acids also was increased but returned to normal sooner than ammonia. The ammonia output is due to an effort of the body to neutralize the acids. The part not neutralized by ammonia appears as increased acid in the urine.

The $p_H$ of the urine was slightly acid or neutral before the fever set in, but with the onset of the fever it became strongly acid. The same but to a lesser extent can be said of the fluids of the tissues.

Phosphoric acid and titratable acid were increased also in a parallel manner.

Carbon dioxide of the blood was decreased in proportion as the acid of the urine was increased.

This tendency to acidosis in fever has been considered the result of an increased output of nitrogen. However, since Beck found an increased output of nitrogen not only in the febrile but also in the prefebrile and postfebrile stage without a corresponding acidosis in the prefebrile and postfebrile stage, he considered this result due to some internal secretory mechanism. The hormones of the hypophysis and suprarenal lead first to an acidosis and then to an alkalosis when injected subcutaneously. Under the influence of fever, there is a change in the normal reaction of the endocrine glands which leads to increased hormone activity, increased oxidation of cells, and consequently to acidosis.

E. W. Erhmann, Chicago.

Influence of a Parenterally Introduced Horse Serum on Metabolism and Composition of the Body. Isamu Watabe, Jahrb. f. Kinderh. **113**:297, 1926.

After a review of the literature the author reports his own experiments, giving his technic in detail. According to his results, the animals gained in weight faster than control animals after repeated injections of serum. Chemical analysis of the rats showed that the gain was due to increase in fat and not to water retention.

Parmelee, Chicago.

The Nucleus-Splitting Ferment of the Pancreas of Nurslings. J. von Lukacs, Monatschr. f. Kinderh. **33**:509, 1926.

Using as an analogy the fact that the production of the ferment lactase depends on the amount of lactose in the diet, the author attempted the same study with respect to the nucleus-splitting ferment of the pancreas. He found that this ferment does not develop until the beginning of the second year. The feeding of material rich in nuclei as thymus does not affect the child's health or cause digestive upsets if given in small quantities in broth earlier than this; but repeated feeding does not cause the appearance of the ferment before the

specified time. The ferment then depends entirely on the child's development for its presence and not on any stimulus from the food.

GERSTLEY, Chicago.

THE EFFECT OF INTRAVENOUS INJECTIONS OF CALCIUM AND POTASSIUM ON THE HYPERGLYCEMIA PRODUCED BY SOLUTION OF PITUITARY. G. MYHRMAN, Ztschr. f. d. ges. exper. Med. **48**:166 (Nov.) 1925.

Myhrman considers the electrolytes important factors in regulating the action of the hormones in particular organs. He cites the antagonistic effects of the potassium and calcium ions on the hypoglycemia due to the administration of insulin, the diuresis due to hypophysial extract and the rise in blood pressure due to epinephrine. The subcutaneous injection of solution of pituitary into animals resulted in a rise in the blood sugar of two types. One rise occurred in one-half hour, reaching a maximum of about 18 per cent in from one to one and a half hours, followed by a decrease below the fasting value; the other type was a small initial rise (3 per cent), which was followed within one hour by a drop below the fasting value. Calcium chloride alone diminished the blood sugar, but the intravenous injection of solution of pituitary two hours later produced a rise greater than that with the solution alone. Potassium chloride alone did not alter the blood sugar, but an injection of solution of pituitary two hours later resulted in a rise in blood sugar greater than with solution of pituitary alone, but not as great as with calcium chloride and solution of pituitary. There was no increase in diuresis during the experiments with the salts.

THE BIOLOGY OF THE SKIN: VI. THE ACTION OF THE INTRACUTANEOUS INJECTION OF INSULIN. E. EDELSTEIN and H. VOLLMER, Ztschr. f. d. ges. exper. Med. **48**:245 (Nov.) 1925.

In answer to E. F. Müller's contention that insulin injected intracutaneously has a more rapid, more intensive and more prolonged action than if given subcutaneously, the results of experiments on a small number of adults are reported. Müller explains his results in part as due to direct parasympathetic stimulation from the skin before any insulin is absorbed. The authors cut off the circulation by applying a tourniquet on the arm and injecting insulin distal to this point. No change in the blood sugar occurred until from fifteen to twenty minutes after the tourniquet was removed. A similar result was obtained with intracutaneous injections of epinephrine hydrochloride. The authors did not find the leukopenia said by Müller to follow an intracutaneous injection of insulin. Müller's report embodies a large series including diabetic cases.

THE CAUSE OF THE LEUKOPENIA FOLLOWING INTRACUTANEOUS INJECTIONS. F. LASCH and A. PERUTZ, Ztschr. f. d. ges. exper. Med. **48**:356 (Jan.) 1926.

There is no leukopenia in the peripheral blood of animals, nor is there any change in the blood pressure following the intracutaneous injection of a foreign protein or saline solution or the stimulation of the vagus electrically or by drugs. Five of sixteen adults reacted to an intracutaneous injection of foreign protein with a decrease in leukocytes of more than 20 per cent (maximum 24 per cent), and a concomitant drop in the blood pressure. In several cases showing diffuse skin lesions the results were negative. The positive reactions

are thought to be the result of a direct parasympathetic stimulation in the skin, resulting in an accumulation of leukocytes in the viscera (liver) and a dilatation of the splanchnic vessels reducing the blood pressure. This relation of the skin to the organism as a whole is absent in animals. In the main the work of Müller is confirmed.

THE RESISTANCE OF THE HEMOGLOBIN OF ADULTS AND INFANTS. H. BISCHOFF, Ztschr. f. d. ges. exper. Med. **48**:472 (Jan.) 1926.

The stability of hemoglobin was tested by adding to 5 cc. of a 1 per cent solution of hemoglobin 2 cc. of fourth normal acetic acid or 1 cc. of fourth normal sodium hydroxide, and determining the time necessary for the disappearance of the characteristic spectrum. The resistance in normal adults was fifty-eight seconds with sodium hydroxide and twelve seconds with acetic acid. In pregnant women the resistance against the hydroxide was increased 25 per cent. Blood from the umbilical cord showed a tremendous increase, the resistance reaching 155 minutes. Full term new-born infants had a value equal to that of the blood of the umbilical cord. Immediately after birth there was a rapid drop; at three months, it was reduced to three minutes (sodium hydroxide), and at one year, to one minute. The immediate rapid drop of the full term infants was absent in the premature infants. The resistance of the hemoglobin of premature infants remained constantly high until an age at which they would have been full term infants. Then the decrease to normal took place.

THE BIOLOGY OF THE SKIN: VII. THE ACTION OF INTRACUTANEOUS INJECTIONS OF INSULIN IN DIABETIC PATIENTS. E. EDELSTEIN and H. VOLLMER, Ztschr. f. d. ges. exper. Med. **50**:297 (May) 1926.

This supplements the previously reported observations in normal adults, and further negates the results of Müller. Intracutaneous injections of insulin in three diabetic children caused no change in the blood sugar, when a tourniquet was applied to the arm used for the injection. Hypoglycemia followed the removal of the tourniquet. The speed of onset and the degree and duration of the hypoglycemia were practically the same with intracutaneous and subcutaneous injections.

M. B. BRAHDY.

EXPERIMENTAL RESEARCHES ON THE INFLUENCE OF HEAT ON THE INFANT. F. DEMUTH, E. EDELSTEIN and H. PUTZIG, Ztschr. f. Kinderh. **41**:1, 1926.

Experiments were undertaken on six infants to determine whether prolonged exposure to high temperatures resulted in any change in the condition or the metabolism which could explain the increased morbidity and mortality during the summer months. Two infants were kept in the warm room at temperatures between 29 and 30 C. and at a humidity of from 50 to 90 per cent for periods of from twenty to twenty-four days in December and January.

Most of the infants stood the heat poorly, and one had a temperature with a classic picture of intoxication when exposed to dry heat. The body temperature, pulse and respiration were elevated in most of the infants. The stools were usually unaffected. The infants secreted a markedly diminished quantity of urine and an increased amount of sweat with resulting injury to the skin in the way of sudamina pustules and furuncles.

The administration of 50 cc. of 2 per cent sodium chloride gave no reaction in the control period and a definite elevation of temperature during exposure

to heat. The administration of 10 per cent of a solution of sugar to the amount of 3 or 4 Gm. per kilogram resulted in the excretion of sugar in the urine during the heat periods in four of six infants. In some cases the motility of the stomach was increased by heat, and the colon bacillus and a more alkaline $p_H$ were found in the stomach. The urinary nitrogen and acidity were measured.

It was concluded that long exposure to high temperatures had a definite influence on the child's organism but that different infants reacted differently to the intensity and kind of heat. It seemed as if younger children responded to the action of heat more mildly. The protocols should be studied by those interested in fever.

BLOOD CHEMISTRY IN EXPERIMENTAL SCORBUTUS IN GUINEA-PIGS. BLOOD SUGAR. I. E. EDELSTEIN and S. SCHMAL, Ztschr. f. Kinderh. **41**:30, 1926.

It was shown by many animal experiments that in scorbutus the blood sugar in a great majority of cases remains unchanged. Only a small number of the guinea-pigs reacted to a lack of vitamin C by a disturbance of the regulation of blood sugar; this disturbance did not occur regularly, nor was the occurrence of a hyperglycemia or a hypoglycemia associated with a definite phase of the disease. A time could not be fixed for the maximum rise or fall of the blood sugar. In agreement with Palladin it was found that small animals were inclined to be hypoglycemic, but this observation also was inconstant.

The calcium and phosphorus values of healthy guinea-pigs fed on a mixed diet showed a fairly large variation — the calcium ranging between 10.1 and 14 and the phosphorus between 6.6 and 10. The calcium metabolism was not influenced by the lack of vitamin C. Phosphorus metabolism was unchanged in most of the animals and in some was definitely lowered.

A MICROMETHOD FOR THE DETERMINATION OF SPEED OF PRECIPITATION OF ERYTHROCYTES. H. LANGER and W. SCHMIDT, Ztschr. f. Kinderh. **41**:72, 1926.

Determinations of the speed of precipitation of red corpuscles have not been made in babies and children because of the amount of blood necessary in repeated tests. A microscopic method which requires only 0.12 cc. of blood is described here, and it seems to be particularly useful in the early diagnosis of tuberculosis and syphilis and may be useful in the diagnosis of various skin diseases.

EMERSON, Boston.

THE RELATION BETWEEN THE COMPOSITION OF BLOOD PLASMA AND EDEMA. J. BOROS and G. CZONICZER, Orvosi hetil. **70**:318, 1926.

The authors have studied the composition of the blood plasma in cases of nephrosis, and their conclusions are that the change of blood plasma as seen in nephrosis may contribute to the causation of edema, but that it seems to be of only secondary importance. For nephrosis, a high concentration of fibrinogen in the blood plasma is characteristic. The protein constitution of the plasma of the patients presents changes in the direction of fractions of rough dispersity. The increase of fibrinogen is a constant phenomenon, probably being in connection with the basic diseases (syphilis, tuberculosis) producing nephrosis. On the other hand, the edema in nephrosis is a variable sign, and there does not seem to be any parallelism between changes of the fibrinogen and edema.

ZENTAY, St. Louis.

EPINEPHRINE HYPERGLYCEMIA IN HEALTHY AND SICK CHILDREN. N. J. SCHIERBECK, Acta Pædiat. **6**:110, 1926.

Blood sugar curves were obtained after the injection of epinephrine following a ten hour fast. The author's conclusions are as follows: 1. Epinephrine hyperglycemia does not occur in fasting children. 2. In normal children the variations in blood sugar may vary from 61 to 177 per cent of the original value. 3. In five rachitic children, curves were obtained which agreed with the highest normal values. 4. Conditions in which the glycogen content of the liver might be supposed to be low gave low normal or subnormal curves: hepatitis, debility, digestive insufficiency, intoxication, convulsive states. 5. In latent tetany, curves below the normal mean were obtained. 6. In three children with weeping facial eczema, low values were obtained. In one case the curve rose after the eczema was healed. In three children with dry eczema and one with ichthyosis, normal values were obtained.

HOLT, Baltimore.

## Nutrition

INFANT FEEDING. CLIFFORD G. GRULEE, J. A. M. A. **87**:137 (July 17) 1926.

The activities of the Infant Welfare Society of Chicago are reviewed. Of 3,293 children under 1 year of age, 26.55 per cent were exclusively breast fed, and 71.5 per cent were exclusively or partially breast fed. Of 1,531 children under 6 months of age, more than one-half were exclusively, and seven-eights were exclusively or partially, breast fed. Only twelve infants had to be weaned for other causes than failure of milk supply before the nine months' period. Cereals and vegetables were extensively used, both as adjuvants to breast milk and as a part of the food given to those wholly artificially fed. Except for the substitution of some other sugar for sucrose, special formulas were used in only twenty-three cases, and acid milks were employed in only twelve of these. The experiences of the society show that seven of eight infants under 6 months of age can be fed in whole or in part on breast milk. In the second six months of life, cereals and vegetables are of advantage in feeding. Acid milks are necessary in only one of 300 cases of infant feeding. It may be necessary to substitute some other sugar for cane sugar in less than 10 per cent of artificially fed infants. There probably is no advantage in the use of proprietary infant foods, and practically no indication for their use.

UPPER RESPIRATORY INFECTION AS A CAUSE OF CHOLERA INFANTUM. PHILIP C. JEANS and MARK L. FLOYD, J. A. M. A. **87**:220 (July 24) 1926.

The authors call attention to mastoiditis and nasal sinusitis as causes of "cholera infantum" and record further evidence, particularly in regard to sinusitis, that these infections are at least a common cause of the clinical picture. Upper respiratory infection is related to the clinical picture corresponding to what has been described under the term cholera infantum. In recent years, all patients presenting this picture to the authors have had either mastoiditis or paranasal sinusitis or both as the apparent underlying cause of their disturbance. The infection seldom is obvious, while the gastro-intestinal symptoms usually are prominent. The establishment of adequate drainage from the site of infection brings about prompt and complete recovery.

BONAR, Salt Lake City.

FEEDING THE NORMAL INFANTS. R. G. McALILEY, J. M. A. Georgia **15**:378, 1926.

In summarizing his paper, McAliley says that the problems of infant feeding should be approached with common sense and a liberal point of view. The objective is the choice of a diet that will promote normal development without producing digestive disturbance or pathologic changes. The best diet is breast milk. It is essential that the mother eat an adequate diet to produce good milk.

Artificial formulas are based on caloric need, protein and fluid requirement. Vitamins and minerals must be added when necessary.

MASHBURN, Atlanta.

THE USE OF SOUR MILK IN INFANT FEEDING. E. P. BAUMANN, M. J. South Africa, September, 1926.

The author briefly sketches the history of sour milk, stating that for 200 years the peasants of Holland used buttermilk as a therapeutic agent in infantile digestive disorders.

The physiology of its use deals primarily with the problem of gastric secretion. By the addition of lactic acid to cow's milk, the buffer substances are neutralized, leaving an amount of free hydrochloric acid in the stomach which more nearly approximates the degree present when human milk is fed, thereby producing a medium in which the action of rennin, lipase and pepsin is of the best.

Lactic acid is stated to be the acid of choice when it is used in its proportions of 1 drachm to the pint. The preparation and clinical uses are discussed, and the author's conclusions are as follows: lactic acid milk by virtue of its cheapness, ease and rapidity in preparation, appears to be the artificial food of choice in all conditions departing from health in early life. The author unhesitatingly confirms the favorable results reported by others.

BUHRMAN, Chicago.

ETIOLOGY AND TREATMENT OF RICKETS. A. SCALA, Ann. d'ig. **36**:526 (July) 1926.

The author regards rickets as a general disease due to the presence in the body of acids or groups of acids which the organism is unable to neutralize and destroy. This condition affects the osseous system most of all because the alkaline defense of bone is insufficient to neutralize these acid bodies. They exert an inhibitory influence on substances whose function is to cause a fixation of calcium salts. Consequently, demineralization occurs. These complex colloidal acids are present in other parts of the body as well as in bone. With this theory in mind, the author treated six children suffering from rickets with a neutral 5 per cent solution of sodium and potassium citrate. The drug was given by intramuscular injection in 1 cc. doses daily for ten days and then was followed by a rest period of ten days. This method of administration was used until forty injections had been given. In conjunction with the citrate the author gave 25 centigrams of calcium lactate by mouth twice a day before meals. There were no dietary restrictions or changes. He noted a marked improvement in all patients treated. The muscles became firm; pallor began to disappear; sleep was more peaceful; walking became easier, and the children appeared brighter and happier generally. No recurrence of symptoms was noted in any of the patients after one year.

BARLOW'S DISEASE IN INFANTS RECEIVING A DIET NOT LACKING IN ANTISCORBUTIC SUBSTANCES. G. ARENA, Clin. Pediat. **8**:407 (July) 1926.

The author presents two cases of infantile scurvy occurring in infants on a diet apparently containing antiscorbutic vitamins. A cure resulted in each case after administration of fresh fruit juices and pure milk.

ZAMBARANO, Northville, Mich.

ANTHROPOMETRIC DEVIATIONS IN RACHITIC CHILDREN 1, 3 AND 5 YEARS OLD. A. PAGANI-CESA, Riv. di clin. Pediat. **24**:749, 1926.

The author measured sixteen rachitic children, 1 year old; thirty-seven 3 years old and seventeen 5 years old. Mean figures for each age are given, and compared with figures obtained previously on normal children.

HIGGINS, Cincinnati.

MASKED FORMS OF SCURVY. SYMPTOMATOLOGY AND PATHOGENESIS. AGAPITO ARGÜELLES TERAN, Arch. españ. de pediat. **10**:513, 1926.

The author believes that there are certain forms of masked scurvy. He designates the condition as prescorbutic or latent Barlow's disease. The principal symptoms are lability of water, equilibrium of the tissue, sharp oscillations and marked disturbance of the weight curve. The state of nutrition is pseudoflorid. There are slight evidences of scurvy, such as pallor, fleeting edemas, retarded motor activity, pains in the joints and erosive gingivitis.

There is commonly a history of insufficient nourishment. Although there is underfeeding, the carbohydrate element predominates in the food. Endocrine lesions are often present. The author advances some interesting theories regarding the mechanism of endocrine metabolism. Dysfunction of the suprarenals due to the scorbutic regimen may be a causative factor. Disturbances in the calcium metabolism may be due to this suprarenal dysfunction and it may also be a big factor in the development of a tendency to hemorrhages.

SCHLUTZ, Minneapolis.

CAUSE OF SEVERAL RACHITIC SYMPTOMS; INFLUENCE OF THE SUN'S RAYS. W. LASCH and MARIANNA MIEMETZ, Jahrb. f. Kinderh. **109**:134 (July) 1925.

That the frequency and intensity of rickets are somewhat dependent on the time of year has been known for a long time. During the winter and spring months (March, April, or even May) rickets has been shown to increase, but after March it usually decreases in intensity and frequency. Hess has shown that there is a direct parallelism between the total number of days of sunshine in a month and the inorganic phosphorus content of the blood. This gives rise to the question of whether the same parallelism prevails under other climatic conditions.

The authors' work was done from April to August, 1923, from the material found in the Infants' and Children's Clinic of Lützowstrasse in Breslau. The results of this investigation are shown in a series of charts which may be summarized as follows:

1. The incidence of rachitic symptoms in the first six years of life was from 84 to 96 per cent; in the first half year in breast-fed infants, from 51 to 86 per cent; in artificially fed infants, from 71 to 86 per cent; in children of

2 years, from 83 to 94 per cent; in those from 4 to 6 years, from 84 to 100 per cent.

2. The highest point of frequency of rachitic manifestations occurred in June with a sinking in July and August.

3. There was a relatively large number of children showing rickets in the first and second month, mostly in April and July.

Symptomatic manifestations include:

Craniotabes was found only in the first year. It was found less often in breast-fed infants than in those artificially fed. The high point usually occurs before April. Rosary is found most frequently in June and July after which it more or less disappears. Deformities of the thorax are seen in the severest forms in the second and third years. The high point of frequency occurs in July. Epiphysial thickening occurs at the distal ends of the bones of the arms; it has its highest point of frequency in July after which it gradually lessens. It also occurs at the distal ends of the bones of the legs and has the peak of relative frequency in May. By June, it is usually on the decline. Bowing of the legs is found almost always in the second half of the first, second or third year. The curve of relative frequency is from April into August. The bowing occurs frequently during the healing period when the child becomes more active. Meteorismus or "frog belly" is considered a symptom of florid rickets.

According to the observations of Hess as well as those of the authors, the beginning of the spontaneous healing of rickets seems associated with the duration and increase of sunshine. Hess found the increase in April. Lash and Miemetz found it in June. This speaks for the probability, therefore, that the time of year is not the important factor, but that the rays of the sun are most important in the spontaneous healing of rickets.

BOHNING, Chicago.

THERAPY OF RICKETS. R. GOLDBLATT; S. ROSENBAUM and F. THOENES, Monatschr. f. Kinderh. **33**:481, 1926.

In studies on fourteen children with well controlled experiments the writers came to the following conclusions: 1. Skin pigmentation is no index of the antirachitic value of ultraviolet therapy. Patients with rickets treated by the quartz light in doses insufficient to cause erythema of the skin did as well as those in whom erythema was produced. 2. The writers confirm the reports of other observers, such as Ludwig F. Meyer, who conclude that ultraviolet therapy is more efficacious than cod liver oil. Attempts at introducing the rays by inunction such as rubbing the skin with irradiated hydrous wool fat were unsuccessful. 3. Giving the rays by means of irradiated milk powder seemed to be more successful. 4. As an index of the progress of treatment, the phosphorus content of the serum is misleading. The roentgen-ray examination is far more satisfactory.

FAVORABLE INFLUENCE OF STOVARSOL ON THE WEIGHT OF NONSYPHILITIC CHILDREN. OTTO TEZNER, Monatschr. f. Kinderh. **34**:6, 1926.

A number of observers have noticed that stovarsol, when used in the treatment of congenital syphilis, seemed to exert an excellent effect on the weight curve of the child. Tezner then determined to try out this drug in the treatment of children suffering with nutritional disturbance. In a certain number of cases, with no other change in diet or treatment, the addition of this drug did exert a decided and favorable influence on the weight curve.

The effect was not due to an increased metabolism, as metabolic studies proved. Likewise, there was no change in nitrogen retention or, if anything, the drug exerted an unfavorable influence. Studies on water and salt metabolism failed to reveal anything of value. However, animal experiments substantiated the clinical observations on growth. Rats fed on stovarsol in addition to the diet showed uniformly better growth and better nutrition than the controls. No effect was noticed on the amount of fat, nor was any influence found on bone growth other than increased size. The drug is not indicated for any of the changes of the bones in rickets.

GERSTLEY, Chicago.

CLINICAL RICKETS. M. KLOTZ, Ztschr. f. Kinderh. **41**:51, 1926.

Contrary to the dictum of György that rickets does not occur in microcephalus, Klotz has seen two cases. Three cases of latent rickets were discovered by accident on roentgen-ray examination after rickets had been looked for carefully and had not been found clinically. One case of congenital rickets was discovered on routine roentgen-ray examination in a new-born child in whom clinical signs were absent.

TOXIC OR DYNAMIC ALBUMIN FEVER. A. REICHE, Ztschr. f. Kinderh. **41**:96, 1926.

There has been a dispute as to the cause of fever in babies following the ingestion of albumin.

Is it due to the peneration of the intestinal wall by toxic bodies which result from the breaking down of protein molecules, or is it the result of the burning up of a rich supply of protein molecules assisted by a diet poor in water?

The giving of sufficient water will bring the fever down. During the course of some experiments on the determination of the speed of precipitation of red blood corpuscles in infants with fever, for the purpose of producing fever, Reiche gave whole milk with 17 per cent sugar and 10 per cent albumin. With human milk, great amounts of albumin could be given without causing a rise in temperature. Human milk will bring down the fever when it has been produced and will also make the children quieter and more satisfied. It exercises a special influence, then, and the fever due to albumin is not a dynamic but a toxic one.

EMERSON, Boston.

## Prenatal Conditions

CONGENITAL OBSTRUCTION IN OESOPHAGUS. H. C. FLOOD, Atlantic M. J. **29**:537, 1926.

The case belongs in the group showing defective development of the esophagus, with atresia and tracheal communication, accompanied by anomalous origin of the great vessels of the heart. The pulmonary artery, after giving off two branches, one to each lung, continued upward and a little outward, forming an arch, and then continued downward as the aorta. It had an opening for the vertebral arteries. The aorta proper emerged as a normal vessel, extended upward for a distance of 2.5 cm., where it bifurcated, forming the common carotid, right and left. Just beneath the right common carotid was a branch, forming the left subclavian. The ductus arteriosis was patulous. A small nodule in the large curvature of the stomach proved to be a piece of pancreatic tissue embedded in the wall.

[ARCH. PATH.]

## Diseases of the New-Born

A Case of Hemolytic Jaundice in the New-Born. R. R. Struthers, Canad. M. A. J. **16**:168 (Feb.) 1926.

This unusual and interesting case presented the following salient features: jaundice of severe type, present at birth, and generally increasing in intensity; enlargement of spleen; increased fragility of red cells; prolonged bleeding time; bile in the stool but none in the urine; greatly increased amount of urobilinogen in urine. On the eighth day, in spite of intramuscular injections of blood and later transfusions, the bleeding became uncontrollable and the baby died.

Postmortem examination showed intense jaundice of all tissues, enlargement of the spleen and absence of obstruction or abnormality in the biliary system. Sections were taken for microscopic examination but were not reported.

Moore, Omaha.

Albuminuria in Infancy: I. Albuminuria in the New-Born. Ernst Faerber and Gunth Suin de Boutemard, Jahrb. f. Kinderh. **63**:259, 1926.

Daily chemical and microscopic examinations of the urine of new-born infants were made in thirty-four cases in a maternity hospital. During the first three days, all the specimens of urine contained albumin, casts and leukocytes, but there was a difference in their characteristics after this time, according to the fluid intake of the babies. As soon as this reached a satisfactory point, the urine became clear. The examinations showed that the albuminuria of the new-born is due to dehydration.

Parmelee, Chicago.

Twitching of the Eyes: A Sign of Intracranial Birth Injury. A. Dollinger, Ztschr. f. Kinderh. **41**:20, 1926.

This symptom, mentioned long ago in the literature and forgotten except in the minds of the laity, and resulting from a special sort of irritation of the motor area, especially in the region of the eye and the facial nerve without other pathologic accompaniments, appears in from one fourth to one third of all babies in the first month, particularly in premature babies, according to Zipperling. It is not physiologic but is an expression of trauma to the central nervous system during birth. It consists of rhythmic, lightning-like deviations of both eyes, in some cases toward the right, in others toward the left, in a horizontal direction with a slow return to the position of rest. There may be few other symptoms of injury at birth. Schwartz and Sigmund were able to find signs of hemorrhage in Deiters' nucleus and in the vicinity of the nuclei of the eye muscle in these cases.

The author thinks it is wrong to assume that these twitchings are of a physiologic nature and of no harmful significance, but he admits that his conviction as to any symptom complex in early infancy, especially in such involved ones as those resulting from birth trauma, is subject to modification. To him it is inexplicable why Zipperling never referred to this sign as nystagmus.

Emerson, Boston.

## Acute Infections

Roentgen-Ray Therapy in Erysipelas. E. S. Platou and Leo Rigler, Arch. Int. Med. **38**:573 (Nov.) 1926.

The authors review the multiplicity and variability of methods of treatment and reason that in a given disease they probably indicate an uncertainty as

to the value of these therapeutic procedures; they say that the lack of uniform success following the employment of such procedures stresses the fact that the disease in question is more or less self limited. To them erysipelas stands out as a striking example of this group of diseases.

Since erysipelas is a self limited disease, they claim that any treatment, to be adjudged effective, must be so in a prompt and definite manner. With this in mind, they compare a series of cases in which careful records were kept of the patients who received roentgen-ray therapy and those who did not. A brief summary is given of eighteen patients who did not receive roentgen-ray therapy but who received the usual routine procedure of magnesium sulphate and glycerin packs. These patients were selected in chronological order, and only those were taken who had no complicating factors to make it difficult to evaluate the treatment.

A second series of twenty-three, taken also in chronological order, were summarized. These patients received the roentgen-ray treatment and with the exception of one death in comparison with four in the nonirradiated group, the drop in temperature was likewise more rapid and the symptoms such as pain, toxicity and general malaise disappeared much earlier than in the patients treated by local application. Only one patient of this series showed any extension of the disease after irradiation and one showed a complication of suppurative cervical adenitis which healed rapidly after incision. The average age in the two groups did not differ materially. The possibility of deleterious effects of irradiation of the skin or hair was considered. In no case was there the slightest tanning of the skin or any effect that could be assigned to the irradiation. The authors also state that "in two cases there was a temporary loss of hair, but this may occur without irradiation." It appears to them that erysipelatous skin is more resistant to irradiation than the normal skin. They give the following summary in conclusion: The present methods of treatment of erysipelas are distinctly unsatisfactory and accomplish little. Roentgen-ray therapy applied to the affected part produces a rapid improvement in both the local and the systemic manifestations, with a reduction of temperature to normal in from one to two days. In a group of patients treated by the routine methods and a similar group treated by roentgen-ray irradiation, the vastly superior results in the irradiated group are shown. Treatment with the roentgen ray is an effective method for shortening the course and decreasing the morbidity and mortality in erysipelas.

LOEBER, New Orleans.

THE CONTROL OF THE COMMUNICABLE DISEASES PREVALENT IN MASSACHUSETTS, WITH A STUDY OF THE MORTALITY DUE TO THEM DURING THE PAST SEVENTY-FIVE YEARS. EDWARD G. HUBER, Boston M. & S. J. **195**:933 (Nov. 11) 1926.

This is the last instalment of this article, which started in the issue of July 8, 1926 (**195**:87).

The purpose was to present as concisely as possible the most approved and effective present-day procedures against the communicable diseases which are notifiable in Massachusetts. The article contains a suggested basic sanitary code for general use. The following are some of the statements made by the author:

"Full control of the communicable diseases seems all but hopeless, for in the final analysis very much depends on the cooperation of the general public."

"By the public is meant not only the laity, but also the medical profession in general, not all of whom have heretofore given their full share of cooperation."

"The laws and regulations concerning the communicable diseases can never accomplish their purpose unless the public obeys them because they are reasonable and proper and not because the police power occasionally punishes a violator."

"Undoubtedly the most effective method of educating the public on health matters is through the schools — primary, secondary and college. The chief thing to teach is the prevention of disease."

"The voluntary agencies, which are always valuable in educational work, can render particularly effective aid in this connection."

"The public health nurse plays almost as important a rôle in health education as the schools. She not only spends most of her time in giving instructions, but she gives them at a time when they are most appreciated. Her work covers the entire range of preventive medicine."

"Information may be gotten before the public in a variety of ways, by printed matter, posters, leaflets, public addresses, movies, the radio, regular health articles in the daily press, and cartoons. 'Scare' headlines must be avoided. The objects of these articles and talks should be to spread information as to the prevention of disease, the manner of spread of the communicable diseases, the necessity of very early isolation, and personal cleanliness."

"Practitioners of medicine may assist the great work in two ways — by giving their patients personal advice on health matters, including advising active immunization, and by full cooperation with the health department."

"Medical societies should remain in active touch with health departments so that they may render immediate aid in the presence of an epidemic. Health departments should be represented on the programs at society meetings."

"Terminal disinfection is not a substitute for concurrent disinfection. Fumigation with sulphur or hydrocyanic acid gas is suitable only for killing insects. Soap and water, air and sunlight, boiling water, and steam, or in short, physical cleanliness, is ample for all except pulmonary tuberculosis — where renovation is thought to be necessary."

"Any child with catarrhal symptoms, fever, marked lassitude, sore throat, skin eruption, cough, cold, sore eyes or any other indication of a communicable disease should immediately either be segregated by the teacher until an examination by the school physician or health department can be made, or should be sent home and the health department notified."

GENGENBACH, Denver.

EPIDEMIOLOGY OF POLIOMYELITIS. W. LLOYD AYCOCK, J. A. M. A. **87:75** (July 10) 1926.

The epidemiologic evidence that poliomyelitis is spread by direct contact is scant, the proportion being about 15 per cent. The author has found on observation of poliomyelitis in Vermont, over a number of years, that recognizable cases seldom occur in such relation to one another that they could be considered as resulting from direct contact. However, the time and space relationships between such cases suggest a more definite relationship than is implied in the abortive, healthy carrier theory of transmission. In a study of multiple cases in families, in the majority of instances the onsets were so close as to suggest simultaneous infection. The idea of simultaneous infection is further borne out by the intervals between so-called contact cases. In New York, in 1916, it was found that additional cases occurring in the same house but not in the same family likewise occurred in the majority of instances within

such a short time of each other as to be considered coincident infection. In Massachusetts, in 1916, the majority of the so-called contact cases (not in the same family) had practically simultaneous onset. From the data presented by the author, he feels that this study suggests that paralytic poliomyelitis is not infrequently transmitted from a given person to other persons within a definite range, but that transmission in such instances is not usually through direct contact between individuals, nor through the intervention of missed cases of healthy carriers, but through some indirect means. This was illustrated in a recent outbreak, the epidemiologic evidence of which pointed to milk as the means of transmission.

SPORADIC MENINGOCOCCUS MENINGITIS. STAFFORD MCLEAN and JOHN P. CAFFEY, J. A. M. A. **87**:91 (July 10) 1926.

Prior to the introduction of serum therapy, the mortality of sporadic meningococcus meningitis approached 100 per cent. Following the introduction of serotherapy, recovery occurred in about 50 per cent. Between the ages of 1 and 5 years, 85 per cent of the patients recovered. In ninety-seven cases of this form of meningitis seen from 1916 to 1926, fifty-nine, or 61 per cent of the patients recovered. The patients varied in age from 35 days to 4½ years. Follow-up examinations were made in forty-four cases. Twenty-five of these have been observed for three years or longer, and in this group fifteen have been observed for from five to ten years. Thirty, or 69 per cent, presented no abnormalties throughout the period of observation. Nine, or 20 per cent, showed serious sequelae, and death occurred in five or 11 per cent. Four were cases of deaf-mutism, two of hydrocephalus, two of impaired vision, and one of mental deficiency. The time of occurrence of sequelae suggests the value of early treatment in their prevention.

SCARLET FEVER FOLLOWING NOSE AND THROAT OPERATIONS. BEATRICE R. LOVETT, J. A. M. A. **87**:96 (July 10) 1926.

Of forty-eight cases classed as surgical scarlet fever, twenty-followed operations, thirteen of which were on the nose and throat. Seven of the thirteen followed operations for cleft palate; two followed resections of the nasal septum, and four followed tonsillectomies. The intervals between operation and the first symptoms of the disease were: in two cases, 2 days; in six cases, 3 days; in two cases, 4 days, and in three cases, a few days. Most of the cases were of the septic type, and complications were numerous, including two cases of bilateral otitis media and unilateral otitis media each, and two of sinus infections. One patient died. In most of the cases of a cleft palate, there was sloughing of the tissues and imperfect closure of the defect, so that the operations were not successful. The occurrence of scarlet fever in children following operations, especially on the nose and throat, suggests the wisdom of testing and immunizing patients beforehand. This was particularly advisable preceding operations for cleft palate.

BONAR, Salt Lake City.

TOXIN-ANTITOXIN. BENJAMIN BASHINSKI, J. M. A. Georgia **15**:386, 1926.

Immunization with toxin-antitoxin mixture is especially useful to the following: (1) All children, from 6 months to 6 years of age, as during this period susceptibility to diphtheria, as well as the mortality, is greatest. This group can be reached in homes, infant asylums, milk stations, day nurseries, kinder-

gartens and orphan asylums. (2) School children from 6 to 19 years of age. Even though the susceptibility as well as the greatest mortality occurs in children under 6, yet these children probably are not brought primarily into contact with diphtheria at its source. School children, on the other hand, usually come into contact with diphtheria each year and carry the infection home. (3) Adults who come into contact with diphtheria and are constantly exposed to the infection, especially physicians, nurses and hospital attendants.

MASHBURN, Atlanta.

THE EARLY DIAGNOSIS AND TREATMENT OF WHOOPING COUGH. BOYD READING, Texas State J. Med. **22**:439, 1926.

The main object in the study of forty-eight undoubted cases was a determination of the value of blood counts in the early diagnosis, and the results of vaccine therapy from a prophylactic and therapeutic aspect.

Most of the patients had been coughing from four to fourteen days before seeking advice. Blood counts were procured at the first visit. The ages ranged from 3 months to 10 years, 60 per cent of the patients being under 2 years.

During the time of this study, many children were seen who had harsh coughs following attacks of influenza.

It was frequently noted that blood taken on the fourth or fifty day after the cough started would reveal a practically normal white cell count, but a decided increase in the proportion of lymphocytes, a definite leukocytosis occurring four or five days later. Examination of the blood between the seventh and fourteenth day after the onset of the cough will reveal these facts in 95 per cent of the cases. This is of much value from the standpoint of prophylactic measures for the exposed child.

Vaccine therapy was given a thorough trial in this series, thirty-one of the forty-eight patients receiving it; the remaining seventeen received antipyrine and sodium bromide mixtures, bromoform, codeine and other remedies, without vaccine. The plain stock glycerol culture of Bordet-Gengue bacilli was used, and the average number of injections was six. The initial dose was 1 billion and the maximum dose 16 billion. The best results were observed in cases showing a distinct reaction; the injections were given every other day.

Efficient vaccine therapy shortens the course of the disease, lessens the severity of the paroxysms and tends to prevent complications. Poor results are obtained by inert vaccine and the administration of too small doses.

Vaccine is an extremely potent remedy as a prophylactic measure. There were twelve exposures in this series. Each patient received four injections. In no instance did pertussis develop in the twelve patients exposed. All injections were started in from one to four days after exposure.

LESLIE MOORE, Dallas.

WHOOPING COUGH AND TUBERCULOSIS. M. F. MOUISSET, Rev. de la tuberc. **7**:592 (Aug.) 1926.

Twelve cases of whooping cough occurred among seventy children between the ages of 5 and 13 years in the Charly tuberculosis preventorium. The disease ran a favorable course in every instance, was of short duration and devoid of complications. Among children residing in the neighboring villages it was less benign and ran a longer course. The author attributes these results to the outdoor life of the children living in the institution.

It was noticed that there was a rapid and marked increase in the circumference of the chest, within physiologic limits, after the onset of the disease, which persisted after recovery. In no case was there any evidence of unfavorable action on a possible antecedent tuberculous process.

SMITH, Ogden, Utah.

BAUER HECHT REACTION VERSUS THE WASSERMANN REACTION. N. PIETRAVALLA, Ann. d'ig. **36**:505 (July) 1926.

The reaction of Bauer Hecht in syphilis is regarded as more sensitive than the Wassermann test. Parallel studies of the two methods were carried out on 3,000 serums. The Hecht test corresponded more closely to the clinical observations than did the Wassermann reaction.

AUTOVACCINATION AGAINST RABIES. V. PINTONI, Ann. d'ig. **36**:569 (Aug.) 1926.

A vaccine made from the brain and cerebellum of animals suffering from rabies was used in the treatment of thirty-two animals bitten by rabid dogs. The treatment was successful in all cases. In 54 per cent of the cases, the bite was around the head and in 66 per cent treatment was instituted during the second week following the bite. The results were better than those obtained by using a fixed virus for every case, since each type may have its own biologic peculiarities and will respond only to an autovaccine made from a virus of its own group.

CUTANEOUS REACTIONS AS A MEANS OF DISCOVERING RECEPTIVITY TOWARD SCARLET FEVER. A. BACCICHETTI, Clin. pediat. **7**:362 (June) 1926.

The author applied the Dick test and the intradermal test with Caronia's vaccine to seventy children whose ages ranged from 1 month to 9 years. He concludes that the Dick reaction with streptococcic toxin reveals the hypersensibility of the skin to the proteins of the hemolytic streptococcus. This hypersensitiveness is an expression of a certain grade of immunity toward the hemolytic streptococcus but does not give the exact valuation of the antibodies present in the blood. As far as immunity is concerned, the Dick test resembles the Pirquet test with tuberculin. It does not reveal the patients who are receptive to scarlet fever.

The intradermal reaction with the Caronia vaccine bears some relation to the immunity for the disease. There is yet to be determined which factor is responsible for the reaction — the protein of the blood serum or the proteins and antibodies of the organism. One can safely say that a positive intradermal reaction does not mean that the patient, when exposed to contagion, will not contract the disease. Much would be learned if the test were carried out with the toxins or bacterial proteins of Caronia's organism without the blood serum.

CLINICAL AND ETIOLOGIC STUDIES ON INFLUENZA. A. PAGANI, Clin. pediat. **8**:257 (May) 1926.

Blood cultures were made from seven cases of influenzal septicemia. A growth was obtained in one case only and the organism died in the third generation. The bacillus isolated from the cultures was avirulent in guinea-pigs, and the author believes that it was a pseudoinfluenzal bacillus as described by Pfeiffer. It is differentiated from the true bacillus of influenza by its lack of virulence in animals.

Fourteen cases showing pulmonary localization of the disease were studied roentgenologically by lung puncture, examination of the sputum and feces, skin tests and blood counts. This was done to determine, if possible, whether tuberculosis played any part in the delayed resolution observed in these cases. The presence of tracheobronchial adenopathy as seen on roentgenograms is an observation that should lead to a suspicion of tuberculous infection; but the absence of enlargement of the hilum by no means excludes tuberculosis. Influenzal lesions of the lungs, especially the bronchopneumonic and scattered miliary-like infiltrations, are often difficult to differentiate from a parenchymal tuberculosis of the lungs. The observations must be correlated with other clinical and laboratory data. Puncture of the lung was done in five cases, and cultures were made of the material obtained. Three were reported negative. In two cases both smears and cultures showed a mixture of micro-organisms but no tubercle bacilli.

Examination of the sputum and feces was negative both as to culture and animal inoculation. The tuberculin test has great value in diagnosis when positive and when correlated with other observations. Its value as a single diagnostic agent is doubtful. The clinical course in six cases pointed to a possible tuberculosis. The skin test was positive in all cases. Each patient, however, made an uncomplicated recovery. Another patient with a negative skin reaction showed an extensive pulmonary tuberculosis at necropsy. The estimation of the number of leukocytes in the blood is of help in many cases. In others its value may be only relative. In all the cases studied, an absolute leukocytosis and a relative polynucleosis were found. While leukopenia is the rule in tuberculosis, many of the cases showed a moderate leukocytosis, probably due to coexistent influenza.

The author concludes that, if any one of these diagnostic methods is positive, due consideration must be given to other data and especial significance to the clinical course and previous history of the patient.

AN EPIDEMIC CAUSED BY A MODIFIED DIPHTHERIA BACILLUS. G. ROI, Clin. pediat. **8**:298 (May) 1926.

An epidemic of diphtheritic rhinitis due to a modified form of diphtheria bacillus is reported. Fifty infants were attacked. Twenty-two were nurslings and eight were newly born, stricken between the second and sixth day of life. Two cases of uncomplicated umbilical diphtheria were observed.

The duration of the disease averaged eight days. Serotherapy was instituted in all cases. For local treatment diphtheria serum and strong silver protein were used. Only one death occurred. There were no postdiphtheritic complications of the nervous system.

The causative organism was isolated from the nose for a long time after clinical cure. The organisms were cylindric and clubshaped, from 3 to 5 microns long and 0.5 micron in width. They showed no tendency toward grouping or filament formation. They were nonmotile. They resisted Gram's stain. Stained by Neisser's method, some of the organisms contained occasional metachromatic granules. Intraperitoneal and subcutaneous injections of the bacteria into guinea-pigs produced no symptoms of disease. They were auto-agglutinable.

The lack of toxicity of the isolated organisms is due to the fact that their virulence was attenuated by residence in the nose. The nasal secretions have a strong bacteriocidal power. That the diphtheria bacillus can, under certain circumstances, lose some of its morphologic characteristics is admitted, but the reasons for this are not clear.

HEMORRHAGIC SEPSIS WITH GRAVE CUTANEOUS MANIFESTATIONS. L. SABBATINI, Clin. pediat. **8**:494 (Aug.) 1926.

A case of septicemia with extensive subcutaneous hemorrhages in a child, aged 3 years, is reported. The onset was characterized by an angina and fever. A few days later, hemorrhagic lesions involving extensive areas of the skin appeared. These proceeded to necrosis and gangrene. No etiologic factor could be determined. Recovery was complete after four months.

ZAMBARANO, Northville, Mich.

THE ERUPTION IN CHICKENPOX. UGO DE GIRONCOLI, Riv. di clin. pediat. **24**:621, 1926.

The author reports two cases of varicella occurring simultaneously in two brothers with a family history of syphilis; on the second and the third days, respectively, of the chickenpox, the two children developed a scarlatiniform eruption, which lasted about fifty hours in one and seventy in the other. Fever lasted only a short time. One boy vomited; there was practically no pharyngitis; the blood counts were 11,400 (45 per cent polymorphonuclear leukocytes) and 9,350 (76 per cent polymorphonuclear leukocytes); there was no subsequent desquamation or albuminuria. The author is inclined to believe that the eruption is a manifestation of the varicella.

HIGGINS, Cincinnati.

LARYNGEAL STENOSIS FOLLOWING MEASLES. MARTIN CALDERIN, Arch. españ. de pediat. **10**:577, 1926.

Conclusions were reached after studying one hundred and fifty-seven cases. The cause of laryngeal stenosis that complicates or follows measles is laryngeal diphtheria in 95 out of 100 cases, in the experience of the author.

Children who have or recently have had measles and who present symptoms of laryngeal stenosis should immediately receive a massive dose of antitoxin (from 25,000 to 30,000 units). Bacteriologic and laryngoscopic examinations in these cases are often negative. The author recommends that every patient with measles should immediately be vaccinated against diphtheria.

Intubation and tracheotomy are serious procedures in measles and should be delayed as long as possible. Intubation is the preferable procedure in the pseudomembranous type of case. Tracheotomy is the better procedure in cases in which there is ulceration or erosion with infiltration and edema and a tendency to abscess formation.

SCHLUTZ, Minneapolis.

VARIATIONS OF THE MEASLES EXANTHEM BY IMPERFECT DEGKWITZ PROTECTION. E. MORO and ELIZABETH MULLER, Jahrb. f. Kinderh. **109**:127 (July) 1925.

If small doses of measles convalescent serum are injected early in the incubation period, one can delay and diminish the illness. According to Degkwitz, such types of measles are characterized by a lack of prodromal symptoms, by a faint or entire absence of rash, by an almost entire absence of catarrhal symptoms, and by the absence of every feeling of illness. Such types are designated as "mitigated measles." In the winter of the last year the authors had the opportunity of observing cases of evident imperfect protective effect after injections of prophylactic serum, in which the measles did not appear to be mitigated but differed in an unusual manner.

Variations that closely resembled the complete clinical picture of german measles occurred in two cases; they evidently were due to the weakening of

the measles organisms by incomplete Degkwitz protection. Concerning the measles exanthem, Pirquet has described the circulation of the infectious sources in the blood, the meeting of these with the antibodies, agglutination, dissolution through lysis, freeing of toxic materials, and toxic reaction about the bacterial foci. In the authors' cases, in which less impulse for antibody action was shown, the spotted form of the exanthem was almost entirely lacking and, in an astonishing manner, the nodular and vesicular types predominated. Probably through the serum, the causative source of the measles was not destroyed but was still so weakened that no strong impulse for the formation of lytic antibodies was given. The specific dissolution was lacking, and the measles organisms had opportunity for the time to grow larger colonies until in some way the natural defenses destroyed them. Nodes, blisters and pustules were formed but not the nodules, which are an expression of the lysis.

BOHNING, Chicago.

DIPHTHERIA. F. V. SZONTAGH-DEBRECEN, Jahrb. f. Kinderh. **113**:184, 1926.

The author is not satisfied with the common view of a diphtheritic infection. Considering autopsy observations in diphtheria, he feels that previous to the local symptoms general changes must have taken place. The local condition is secondary, and the organisms are also secondary. In diphtheria the local symptoms should be given the same importance as the local characteristics in scarlet fever. Observations at autopsy in a large number of cases of diphtheria show that changes of a toxemia are marked, and that these children often die as soon as they become ill clinically.

Consequently, the author feels that because modern serum therapy considers the disease as a primarily local condition it will fail sooner or later.

BACTERIOLOGIC OBSERVATIONS IN BRONCHOPNEUMONIA OF MEASLES. NORBERT HEMING, Jahrb. f. Kinderh. **113**:217 (July) 1926.

During an epidemic of measles, which broke out in the children's home of Froebel Street in Berlin, in 1922, Heming examined about thirty-nine patients post mortem, all of whom died of bronchopneumonia. Hemolytic streptococci were grown from the lungs of these patients. In following epidemics he made pharyngeal smears as well as blood agar plates from material coughed up. This was done by holding the plate in front of the child's mouth as it was made to cough by placing a spatula in its mouth. From his observations, Heming concluded that streptococci are found on the "cough plates" only in cases complicated by bronchopneumonia. Twelve patients, all of whom showed hemolytic streptococci, died; four had pneumonia, and one of these died. Even in cases of primary measles, hemolytic streptococci of pneumonia was found, which destroy the idea of a primary pneumonia due to the measles virus.

E. W. EHRMANN, Chicago.

THE EPIDEMIOLOGY OF GERMAN MEASLES. HASSELMANN-KAHLERT, Monatschr. f. Kinderh. **34**:35, 1926.

An epidemic of German measles occurring in a ward of patients with scarlet fever is described. Of twenty patients, twelve developed German measles. The disease is therefore not so highly contagious. In all cases the incubation period was from eighteen to twenty days. Five children did not develop the disease on the first exposure, but developed it later following infections of otitis and pharyngitis, which apparently lowered their resistance.

VACCINE ENCEPHALITIS. IRENE KOLLAR, Monatschr. f. Kinderh. **34**:51, 1926.

Kollar reports a case of encephalitis apparently following vaccination. The duration of the encephalitis was three months, with recovery.

GERSTLEY, Chicago.

CAUSE OF DEATH FROM DIPHTHERIA. F. M. BRICKER, Ztschr. f. d. ges. Exper. Med. **48**:444 (Jan.) 1926.

The functional capacity of isolated arterial segments from the various organs was studied by the reactions to various stimulating drugs (epinephrine, caffeine), after animals had been infected with diphtheria. In the acute intoxication, vascular changes were marked, except in the pulmonary vessels, which retained the power of dilatation. In the subacute cases the peripheral, intestinal and cardiac vessels were less affected than in the acute cases. Anatomic and functional changes do not run parallel. The author stresses the paralysis of the coronary arteries, and thinks the direct injury to the arteries in general is the primary cause of death, the cardiac insufficiency being secondary.

M. B. BRAHDY, New York.

A CASE OF PRIMARY DIPHTHERIA OF THE OUTER EAR. CORNELIUS VEITS, Ztschr. f. Hals-, Nasen- u. Ohrenh. **16**:33 (July 31) 1926.

The author describes a case in point. A woman, aged 41, had had a furuncle in the outer canal of the left ear which had been incised, Jan. 5, 1925. The patient again came to the clinic one week later. The area of the former abscess, which reached to the cochlea, was reddened and swollen. During the next days the eczema spread to the outer and posterior portion of the auricle and toward the angle of the jaw. Grayish brown-black crusts had formed; the rest of the canal was filled with a grayish white mass. After one week, the corium and the cartilage at the helix and tragus were laid bare. On February 15, fetid pus was present. The operation of removing the crust led to excruciating pain and hemorrhage. Nine days later, the patient received 0.45 Gm. of neoarsphenamine intravenously.

In 1909, the patient had attempted to commit suicide by swallowing numerous needles, and a laparotomy had been performed at that time. The patient said that on Dec. 30, 1924, she had scratched the ear with a needle, and that a child had pushed her which had caused the needle to enter the canal. In November, 1925, three needles could be seen in the roentgenogram. On November 24, two whole needles were removed. The one in the throat was covered by the external jugular vein; the outer end of the other was in the sternocleidomastoid muscle. The disease lasted more than six months, while cases described so far had had a duration of only from two to eight weeks. The unfavorable tendency to heal was probably a consequence of angioneurosis. Three relapses occurred on the left side. Later, otitis externa developed on the other side also, with grayish white pseudomembranes and violent pain. The pain disappeared almost immediately after a dose of 2,000 units of bovine diphtheria serum had been given. Within twelve days, five additional injections were given. The patient suffered from hysteria and vasoneurosis.

Veits states that diphtheria of the canal of the outer ear develops from the middle ear, or follows an injury or another inflammation (Kraussold, Gruber, Baginsky). The infection through foreign bodies has not been described so far. Perhaps the patient, who was a carrier, had infected the needle by

moistening the thread while sewing. It was difficult to influence the process therapeutically. Acriflavine was used. Diphtheria serum was applied subcutaneously. Neoarsphenamine, permanganate of potassium and mercurial ointment were used. Acriflavine and diphtheria serum, applied locally, seemed to be ineffective. Diphtheria serum used parenterally was of surprising effectiveness, especially at its first application. The pain disappeared immediately, and most of the membrane could be removed the next day. Healthy granulations appeared, so that at first two injections appeared to control the process, but this was not the case. As anaphylactic symptoms were feared at the next relapse, the serum was used locally but without result. An injection of a flavine dye was also without result. When the process appeared in the other ear, bovine diphtheria serum was used. The pain disappeared promptly, while the objective picture was scarcely changed. This relief from pain, caused by the serum without influencing the fever and other symptoms in diphtheria of the middle ear and of the external auditory canal, has also been observed by Daae. In similar cases larger doses might be recommended. A larger dosage of bovine diphtheria serum could not be obtained for the patient. Permanganate of potassium and especially mercurial ointment (Hilgenreiner) seemed to have a decidedly favorable influence on the fetid odor.

AMBERG, Detroit.

THE DICK TEST. J. BOKAY and B. JOHAN, Orvosi hetil. **70**:79, 1926.

The authors report their experiences with a large number of children. Their conclusions are as follows: 1. The results obtained with the Dick test are practically identical with those of American authors. There seems to be a definite connection between the positive test and susceptibility for scarlet fever. The test is without danger. The solution of toxin used should be absolutely reliable, and the technic of the intracutaneous injections should be faultless. 2. Active immunization with toxin produces a negative Dick test in a great majority of cases. Further experience is necessary to clear up the question of duration of this immunity. With a reliable solution of toxin and with proper dosage the procedure is without any danger. The occasional toxic erythema has no serious significance and usually is mild in character. This toxic erythema should not be considered as a rash of scarlatina. 3. The work of Drs. Dick is important in solving the problem of the causation of scarlet fever.

THE VALUE OF SERUM TREATMENT IN DYSENTERY. K. KALOCSAY, Orvosi hetil. **70**:218, 1926.

Polyvalent specific serum was used in dosage ranging from 50 to 100 cc. The author thinks that early injection of the serum has a favorable effect on the course of the disease. After the second or third day, there is practically no effect.

ZENTAY, St. Louis.

PROGRESSIVE MUSCULAR ATROPHY WITH CONTRACTURES FOLLOWING ABDOMINAL TYPHUS IN TWO ADOLESCENT BROTHERS. LADISLAV HYBNER, Čas. lék. česk. **64**:935 (June) 1925.

Involvement of tissue of the nerves such as occurs in meningitis, encephalitis, myelitis and polyneuritis, is not uncommon following typhus. A rare muscular involvement is described in two brothers, aged 15 and 22, taking place six and thirteen years, respectively, after the acute infection. There was a gradual atrophy of the upper and lower extremities and the muscles of the neck and torso. Contracture deformities occurred, which were partially overcome by

tenotomies about the elbow and ankle. Pseudohypertrophic tendency, myositis with degeneration, abscess formation or other less rare posttyphus changes in the muscles were not demonstrated. Familial idiopathic dystrophy was not considered because of the difference in the age at onset and because of the typical clinical picture.

STULIK, Chicago.

MUMPS MENINGITIS WITHOUT PAROTITIS. ARVID WALLGREN, Acta Pædiat. **6**:53, 1926.

Mumps meningitis is not a rare occurrence in Scandinavia. Although the meningeal symptoms may be severe, as a rule they are mild, considering the pronounced changes that are found in the spinal fluid. The typical observations on lumbar puncture are a clear or faintly turbid fluid with from 50 to 250 mononuclear cells, but with only a slight reaction for globulin. The meningeal symptoms usually develop after the parotitis, but they may be the first manifestation of mumps.

The author reports several cases of meningitis in which the parotitis was of a transient character—a slight tenderness to palpation over the parotid or submaxillary glands being noticed for a day or two during the course of a definite mumps meningitis. In one case, there was no evidence of parotitis at all, although it seemed clear from the epidemiology that the case was one of mumps: the oldest of three brothers had a typical attack of mumps. Three weeks later, the two younger brothers were taken sick. One of them had a typical parotitis with meningeal symptoms, while the other had a typical attack of meningitis, such as is characteristic of mumps, with no evidence whatever of involvement of the salivary glands. Four similar instances were found in the literature.

The author believes that a mumps infection may be the cause of some of the perplexing cases of benign serous meningitis that are occasionally seen.

INTRADERMAL INOCULATIONS WITH FILTRATES OF STREPTOCOCCI FROM SCARLET FEVER AND OTHER SOURCES. G. JACOBSOHN, Acta Pædiat. **6**:67, 1926.

Filtrates from thirty-four strains of streptococci from various sources were tested on patients with positive and negative reactions to the Dick test. The results were consistently negative; only occasionally was a doubtful or positive reaction obtained. One strain of streptococci was obtained from a throat that gave reactions identical with the Dick test.

The author finds that hemolytic streptococci are present with equal frequency in the throats of persons with negative and positive reactions to the Dick test.

HOLT, Baltimore.

## Chronic Infections

THE CONTAGION OF TUBERCULOSIS. EUGENE L. OPIE and F. MAURICE MCPHEDRAN, Am. Rev. Tuberc. **14**:347 (Oct.) 1926.

When latent tuberculosis is taken into consideration, tuberculosis exhibits the characters of a contagious disease and affects all children of households in which some member scatters tubercle bacilli. With the recognition of latent apical tuberculosis, it has been demonstrated that the infection is transmitted to adults and to adolescent children, and that approximately one half of the partners of husbands and wives with open tuberculosis are infected after marriage. In instances of recognizable tuberculosis of the tracheobronchial lymph nodes, the average duration of contact with tuberculosis has been

approximately four and one-half years, and in latent apical tuberculosis nearly twice as long. Latent tuberculosis often becomes manifest. During the first two years of life, children with positive tuberculin reactions, with roentgenologic evidence of tracheobronchial tuberculosis, or with latent apical tuberculosis during adolescence should be treated as though they had recently arrested tuberculosis. Adults with latent apical tuberculosis should receive the same care as patients with arrested tuberculosis.

CLINICAL RECORDS CONCERNING THE EXPOSURE OF CHILDREN TO TUBERCULOSIS. L. F. RICHDORF and A. E. HETZLER, Am. Rev. Tuberc. **14**:420 (Oct.) 1926.

The value of a history of positive exposure to tuberculosis depends on a definite diagnosis of active and open disease in adult contacts. In the group of children studied, evidences of infection occurred twice as often in the exposed as in the unexposed. Children showing primary foci in roentgenograms of the lungs usually but not always gave a positive Pirquet reaction.

SERIAL EXAMINATIONS OF CHILDREN WITH EVIDENCES OF PRIMARY FOCI. F. LEGGETT, DOROTHY HUTCHINSON and J. A. MYERS, Am. Rev. Tuberc. **14**: 428 (Oct.) 1926.

Serial examinations of children with tuberculosis revealed areas interpreted as primary foci in the following locations: right upper lobe, 9; right middle lobe, 3; right lower lobe, 17; left upper lobe, 13; left lower lobe, 13.

In all cases the focus was apparently calcified and the hilum nodes enlarged, with evidence of calcification in all except three. Calcification was usually more marked on the side of the primary focus. Three cases showed two or more foci.

While no changes in the primary lesions have been noted during the course of these observations, the authors are convinced that in time some may heal by resolution, leaving no demonstrable trace of their former existence. Several cases in this series, which when first observed showed changes in the lungs which seemed to warrant an unfavorable prognosis, on subsequent examinations have shown marked and progressive improvement.

TUBERCULOUS INFECTION AMONG MINNEAPOLIS SCHOOL CHILDREN AS REVEALED BY THE INTRACUTANEOUS TEST. F. E. HARRINGTON and J. A. MYERS, Am. Rev. Tuberc. **14**:454 (Oct.) 1926.

Intracutaneous tuberculin tests were made on 2,188 Minneapolis children of school age. The first test was made with 1 minim of a 1:1,000 solution of tuberculin. About a week later, those who reacted negatively were given 1 minim of a 1:100 solution. No stronger dilutions were used. Of this number 776 reacted positively to the 1:1,000 dilution, and of the negative reactors, 229 had positive reactions with the 1:100 dilution. The percentage of positive reactions in the entire group was 48.76 among the boys and 45.89 among the girls.

SERIAL EXAMINATIONS OF INFANTS SHOWING POSITIVE TUBERCULIN SKIN REACTIONS WHILE UNDER TWO YEARS OF AGE. H. F. WAHLQUIST and J. A. MYERS, Am. Rev. Tuberc. **14**:461 (Oct.) 1926.

During the last two years, seventy-one children up to 2 years of age, who have had tuberculous infection as revealed by the Pirquet test, have been followed. A history of familial exposure was obtained in 95.7 per cent. Inter-

scapular dulness was found in 46.5 per cent. Constitutional signs and symptoms, such as fatigue, loss of weight or failure to gain, weakness and fever, were present in 30 per cent. The roentgenograms showed changes in the chest, particularly in the region of the hilum, in 40.8 per cent. The mortality from tuberculosis in this group so far has been only 8.4 per cent. The prognosis of simple tuberculous infection in infancy therefore seems not to be so grave as it was once considered. A positive tuberculin reaction, even in infancy, does not necessarily indicate an active tuberculosis, but merely a tuberculous infection.

A Study of the Lung Hilum in a Group of Children Examined for Tuberculosis. H. A. Burns and J. A. Myers, Am. Rev. Tuberc. **14**:468 (Oct.) 1926.

Prior to the development of the roentgen-ray and skin tests, it was impossible to recognize the earliest manifestations of tuberculosis; the secondary or lymphatic stage was diagnosed only when the superficial glands became involved, and the entire problem of diagnosis, treatment and control was limited to the third stage, that of invasion. The application of these tests has enabled the present day clinician to follow the disease from its point of entrance, through all of its stages, until its classic pathologic course has developed its classic symptomatology. The skin tests have already become an accepted and reliable procedure. The interpretation of roentgenograms of the chest still requires standardization. The primary focus can be demonstrated only when fibrosis or calcification has taken place. Adenopathy of the tracheobronchial lymph nodes may result from various conditions other than tuberculosis. These, however, are usually of an acute nature, and the adenopathy tends to disappear when the cause is removed. Serial roentgenograms showing persisting enlargement, and especially calcification, strongly suggest tuberculosis.

In a group of 1,165 children up to 14 years of age, with known exposure and suggestive physical signs, 947 had calcification of the hilum; in 849 the hilum was moderately enlarged, and in nineteen it was greatly enlarged. Primary foci were demonstrated in 231. The hilum shadows were normal in 180 roentgenograms.

Stereoscopic roentgenograms of thirty-one of these children under 2 years of age showed calcification of the hilum in five, calcified primary foci in two, enlarged hilum shadows in thirteen, and a normal hilum in twenty-eight. Disseminated tuberculosis has not occurred in any of these children, and they seem to be doing as well as others infected later.

Smith, Ogden, Utah.

Syphilis of the Bronchial Glands. A. B. Marfan and Jacques Debray, Nourrisson **14**:285 (Sept.) 1926.

A rachitic infant at the age of 4 months developed a stridor that was much more marked during expiration than inspiration. Roentgenograms revealed a persistent shadow at the hilum which was interpreted as enlarged bronchial glands. Repeated tuberculin tests were negative. On the suspicion that both the rachitic deformities and the enlarged bronchial glands might be due to a congenital syphilis, the patient was treated with ultraviolet irradiation, neoarsphenamine and mercury. The stridor gradually subsided, so that at the age of 16 months it was barely audible. An attack of measles at the age of 20 months was followed by a rapidly fatal bronchopneumonia. The postmortem examination, in addition to the recent pneumonic lesions, revealed large bronchial glands, which on section showed characteristic lesions of syphilis and the absence of any tuberculous taint. There was a marked sclerosis and an oblitera-

tive arteritis, with round cell infiltration. The authors point out that a stridor predominating during expiration points to a compression of the lower trachea or of a large bronchus.

McClelland, Cleveland.

Congenital Syphilis of the Long Bones in Infancy. M. Péhu and Madame J. Enselme, Rev. franç. de Pédiat. **1**:261 (Sept.) 1925.

Of what types are the syphilitic lesions of the bones encountered by the pediatrician, and with what frequency to they occur? The authors, in their infants' service, had the opportunity to study forty cases of syphilis during a period of three years. Thirty of these showed involvement of the bones; 50 per cent of these showed a periostitis, 30 per cent an osteochondritis, 13 per cent a form designated as osteoclastic and 6 per cent a gummatous formation. In general the types were mutually exclusive.

Careful clinical and roentgenographic studies were made, and in some cases autopsy material was available. In the discussion of the various forms, a full review of the literature is given. Under the head of osteochondritis, the authors emphasize the vascular distribution of the spirochete early in fetal life, the rarity of the condition after 6 months of age, and the proliferative rather than the degenerative nature of the process. They disagree with those who claim an epiphyseal separation in severe cases, maintaining that the break really occurs in the metaphysis. In cases of periostitis, they found sleeve-like thickening of the periosteum. Another type of periostitis, in which there was a thin space separating the periosteum from the cortex, developed in some cases during the course of treatment. Gummas rarely progress to suppuration in infants and must be diagnosed by the roentgen ray. The osteoclastic type includes the infants showing frequent fractures or unusual flexibility of the bones. In some of these the roentgenogram showed no abnormality, but in others it revealed a loss of substance corresponding to a bony destruction.

The authors verify the observation that the osseous lesions in congenital syphilis occur in the bones formed in cartilage rather than in the membranous bones, and also that osteochondritis (of the Wegner-Parrot type) and the generalized ossifying periostitis are pathognomonic of congenital syphilis and do not occur in acquired syphilis, no matter how early the infection has taken place.

Leslie, Chicago.

Cerebrospinal Fluid in Tuberculous Meningitis in Infancy. G. Tacone, Clin. pediat. **7**:321 (June) 1926.

1. The pressure of the spinal fluid in tuberculous meningitis is almost always increased. It is also frequently increased in whooping cough, intestinal toxicosis and pneumonia.

2. The fluid of meningeal tuberculosis is usually colorless, although it may be hemorrhagic or xanthochromic. Ordinarily limpid, the fluid is sometimes turbid or purulent.

3. The fibrinous reticulum forms constantly. It has also been seen in post-diphtheritic paralysis, Heine-Medin disease, lethargic encephalitis and syphilitic meningo-encephalitis.

4. The fluid is hypotonic in tuberculous meningitis, but this characteristic is not constant or pathognomonic.

5. Meningeal permeability is increased.

6. The absence of peroxidase, often diagnostic of tuberculous meningitis, is, however, a common observation in syphilitic meningitis, dementia paralytica and cerebral syphilis.

7. The enzyme reaction is not adaptable to the diagnosis of tuberculous meningitis, although it is frequently positive. Many cases of extrameningeal tuberculosis show the same reaction.

8. Diminution of chlorides is a common observation in tuberculous meningitis.

9. Hyperalbuminosis is present, as it is in other types of meningitis.

10. Reducing substances are diminished or absent.

11. Increased globulin is a constant observation. Its presence may be determined by the methods of Noguchi, Nonne, Apelt, Boveri and Pandy. If the Boveri and Pandy tests are negative, tuberculous meningitis is excluded.

12. The Aiello reaction is constantly positive, but a negative reaction does not exclude tuberculous meningitis.

13. The bichromate of potassium reaction, although not specific, is positive in tuberculous meningitis. Its negativity rules out the disease.

14. The cytology of the fluid is important. Lymphocytosis is a common observation. Polynucleosis occasionally occurs.

15. Bacteriologic examination is of absolute importance and is really the only true diagnostic feature. Repeated examinations often are necessary to find the tubercle bacillus.

THE LEUKOCYTES OF THE BLOOD IN MILIARY TUBERCULOSIS. G. HALFER, Clin. pediat. **8**:400 (July) 1926.

In miliary tuberculosis the neutrophils are profoundly altered by the tuberculous process. They are not young, nonsegmented forms, but are mature forms whose vital processes, especially the segmentation of the nucleus, have been arrested by tuberculous toxins. In this disease the nonsegmented neutrophils are increased. There is a marked absence of acidophilic cells (total aneosinophilia). Diminution of the lymphocytes is marked. Many lymphocytes contain azurophilic granulations. Gumprecht's astructural cells are present. There is a leukopenia or a normal total number of white cells.

ZAMBARANO, Northville, Mich.

CLINICAL AND PATHOLOGIC CONSIDERATIONS REGARDING TUBERCULOUS MENINGITIS IN CHILDREN. ENZO OMI, Riv. di clin. pediat. **24**:591, 1926.

The author has assembled and studied the data obtained regarding 261 cases of tuberculous meningitis seen in the pediatric clinic at Bologna between 1903 and 1925; autopsies were performed on fifty-four of the patients. Of the 247 cases in which a family history could be obtained, in 112 there was a probable focus of infection in some other member or members of the family. There were 126 boys and 135 girls. Only forty-six of 250 patients gave a definite history of a previous illness due to tuberculosis.

Fifty-seven children had suffered from an acute infectious disease within one year of the onset of the meningitis; 27 had had measles; 6, pertussis; 4, scarlet fever; 2, diphtheria; 8, influenza; 7, chickenpox and 3, typhoid fever. Seventy-two cases occurred during the winter, 102 in the spring, sixty in the summer and twenty-nine in the autumn. Although clinical examination showed tuberculous tracheobronchial glands in only 25 per cent of the cases, at necropsy involvement of these glands was found in 97.5 per cent.

HIGGINS, Cincinnati.

STRIDOR DUE TO LARYNGEAL SYPHILIS. ALFREDO CASAUBON, Arch. latino-am. de pediat. **20**:561, 1926.

This case report concerns a child, aged 3 years, in whom laryngeal stridor was a pronounced symptom. An accompanying acute tonsillitis with symptoms of croup masked the true condition and had led to a diagnosis of laryngeal diphtheria for which antitoxin was given.

A direct laryngoscopy and a four plus Wassermann reaction revealed the true nature of the condition. There was complete absence of any other syphilitic manifestation. Antisyphilitic treatment promptly cleared up the condition.

SCHLUTZ, Minneapolis.

THE USE OF THE BLOOD PLATELET CURVE AS AN INDEX OF THE ACTIVITY OF A TUBERCULOUS PROCESS. HANS SCHLACK, Monatschr. f. Kinderh. **33**:504, 1926.

Degkwitz has reported that in normal persons or in persons with positive tuberculin reactions but clinically well the parenteral injection of protein results in no change or in a slight increase of the blood platelet count. In active tuberculosis the count falls. The author was not able to confirm these observations. In scrofula there was an increase in the platelet count almost with no exception.

GERSTLEY, Chicago.

SIGNIFICANCE OF SUPERINFECTION IN THE COURSE OF TUBERCULOSIS IN CHILDHOOD. H. LANGER, Ztschr. f. Kinderh. **41**:63, 1926.

Superinfection is an infection with tuberculosis repeated at a time when the first one has not yet resulted in a biologic change in the sense of an increase of resistance. It is an infection repeated at a short interval. It is important in the first year of life and varies with the amount of exposure in that the mortality of tuberculous infants in infected families is twice as great when both parents are infected than when only one has the disease. Infants who were nursed a long time by infected mothers all died. Reinfection is an infection in children that occurs a long time after the first one, so that some resistance has been built up. Reinfection occurs usually after the first year. The avoidance of superinfection is more important than the avoidance of reinfection.

EMERSON, Boston.

DISTURBANCES OF MENTAL DEVELOPMENT IN CONGENITAL SYPHILIS WITH CEREBROSPINAL FLUID OBSERVATIONS. GÖSTA ÅHMAN, Acta Pædiat. **6**:1, 1926.

Åhman reports eighty-six cases of congenital syphilis. Changes in the spinal fluid were found in two thirds of the infants and in about one fourth of the older children. The author believes that the diagnosis of neurosyphilis cannot account for the high percentage of feeblemindedness in syphilitic children. Syphilis of the endocrine glands may be responsible for many of these cases.

HOLT, Baltimore.

## Internal Diseases

COR BIATRIATUM TRILOCULARE. C. ALEXANDER MCINTOSH, Am. Heart J. **1**:735, 1926.

A case of multiple cardiac anomalies — cor biatriatum triloculare — is described which presented the following anatomic characteristics: mitral atresia, absent intraventricular septum, hypertrophied pulmonary artery becoming the

descending aorta through a patent ductus arteriosus, extreme hypoplasia of the aorta, solitary (left) coronary artery, bicuspid aortic valve, accessory pulmonary vein leading from the upper portion of the right lung to the superior vena cava, anomalous communication between the left auricle and the superior vena cava.

AUTHOR'S SUMMARY.

BLOOD SUGAR IN STATUS THYMICOLYMPHATICUS. AUBREY B. MACLEAN and RUTH C. SULLIVAN, Am. J. M. Sc. **171**:659, 1926.

In three cases of status thymicolymphaticus the blood sugar values were low (42, 52, 57 mg. per hundred cubic centimeters). In one case of suprarenal hemorrhage a blood sugar of 25 mg. per hundred cubic centimeters was found. In six cases of convulsions produced by conditions other than status thymicolymphaticus the blood sugar contents were normal or increased above normal. In six cases of enlarged thymus shown by roentgenograms, the blood sugar was within normal limits in five and slightly decreased in one. In six cases in which the blood sugar was determined within half an hour before death in patients with diseases other than status thymicolymphaticus, the values were normal or above normal.

Acute suprarenal insufficiency is suggested as the immediate cause of sudden death in status thymicolymphaticus.

AUTHORS' SUMMARY.

SERIAL EXAMINATIONS OF CHILDREN WITH PULMONARY LESIONS. DOROTHY HUTCHINSON and J. A. MYERS, Am. Rev. Tuberc. **14**:437 (Oct.) 1926.

If roentgenograms of the chest were made of all children with obscure ailments, many would be found to show pulmonary lesions which would be overlooked otherwise. Physical signs may be slight or absent. Cutaneous tuberculin tests, while usually positive, may be persistently negative, may become positive after a previous negative test, or may become negative in cases at one time positive. Serial examinations of children with evidences of pulmonary tuberculosis frequently show remarkable recoveries in the younger groups. Undoubtedly many mild cases run their course undiagnosed in most of them improvement taking place. Nine cases in this group of sixty-five showed complete healing or calcification of the lesions, with disappearance of all clinical signs and symptoms.

SMITH, Ogden, Utah.

RENAL DWARFISM. REPORT OF A CASE. FREDERIC W. LATHROP, Arch. Int. Med. **38**:612 (Nov.) 1926.

The author calls attention to the rarity of the association of chronic nephritis with changes in the bone in adolescents. He reviews the literature and gives credit to the British medical world for the number of cases described in the British literature and points out the paucity of cases recorded in American journals.

He reports the case of a girl, aged 15, admitted to the Johns Hopkins Hospital, April 6, 1925, one of the youngest of a family of ten children, all living and well. The onset of the present illness began definitely at the age of 12, two and a half years before admission. The onset of the symptoms is typical and is the same as described by the British authors. The author deplores the fact that the British authors have not furnished any figures as to the chemical constituents of the blood that he might use for comparison. The more striking observations in the case that he was able to observe for two

and one-half years before death were that the nonprotein nitrogen was 74 mg. per hundred cubic centimeters for to and one-half years before death, and that for more than a year repeated observations showed that it was constantly about 100 mg. The creatinine also was surprisingly high over a long period. The calcium and phosphorus figures show a complete reversal of the normal values. Calcium was about 5 mg. and the phosphorus was more than 9 mg. The author called attention to the fact that one of the big problems in this case was the absence of tetany in spite of a blood calcium of less than 5 mg. At no stage was there the slightest clinical evidence of tetany, though on frequent occasions attempts were made to elicit Chvostek's and Trousseau's signs. Acidosis with a carbon dioxide capacity of 30 per cent by volume was notable in the absence of hyperpnea or any other untoward symptoms.

The pathogenesis of the deformity of the bone was interesting. Clinically the genu valgum, rachitic rosary and thickened epiphyses were difficult to differentiate from similar deformities found in true rickets. At necropsy, microscopic examination of the costochondral junctions shows in some places an irregularity of the epiphyseal line with osteoid tissue similar to pictures seen in true rickets. However, the roentgenograms show nothing suggestive of rickets. The picture is merely that of delayed ossification. There is not the irregularity of the epiphyseal line that is seen in that disease, and there is none of the density of an old healing process. The kidneys were extraordinary in appearance. They were both distorted pieces of tissue which hardly resembled kidneys externally. An extreme reduction of kidney substance was found with some areas resembling chronic nephritis but associated with chronic pyelitis and chronic cystitis.

In the patient described, all the characteristic symptoms as given in previously reported cases were present; i. e., the insidious onset in the second decade, the nausea and occasional vomiting, frontal headaches, dwarfism, knock-knee, polydipsia, polyuria and nocturia, with anorexia, air hunger and uremic coma as the terminal events. The physical examination also was similar, showing as it did dwarfism, absence of secondary sexual characteristics, normal blood pressure and normal sized heart, genu valgum, rosary and thickening of the epiphyses, a urine of low specific gravity and albumin with few casts, a low phthalein excretion, and increased nonprotein nitrogen of the blood.

The author summarizes his case as follows:

1. In the case of renal dwarfism reported here, the patient presented the picture of a severe renal insufficiency in association with a curious failure of the development of the bones.

2. Phosphate retention with resulting low blood calcium over a long period may be the cause of the delayed ossification of the bones.

3. The severe acidosis may have been the factor in causing the ionization of a sufficiently large proportion of the calcium to prevent the onset of tetany.

ARACHNIDISM. SPIDER POISONING: REPORT OF A TYPICAL CASE. EMIL BOGEN, Arch. Int. Med. **38**:623 (Nov.) 1926.

The author reports as typical one of a series of fifteen patients who were treated for bites by poisonous spiders at the Los Angeles Hospital in recent years. They were all males ranging in age from 2 to 65, more than half being young adults. The author reviews the literature and the treatment of bites of spiders not only in America but in many foreign countries besides. He states that more than 150 cases of bites of poisonous spider have been reported by thirty-three physicians in the United States during the last century. Two

thirds of these occurred in California, but the others were scattered over more than a dozen states, including Florida, Virginia, Georgia, North Carolina, Alabama, Texas, Oklahoma, Maryland, Pennsylvania, Tennessee, Ohio, West Virginia and Arkansas. All ages have been reported; all classes of people have been attacked, and any exposed part of the patient has been bitten.

There has been no special time of day and no special month of the year for the bites to occur. The spider actually causing the bite was captured and identified by arachnologists in about a dozen cases. It was usually described as a shiny black spider, and a spot on the abdomen was frequently mentioned. A stinging or sticking sensation was noted at first, but this soon disappeared, and except for a tiny red spot sometimes seen, there was no mark or swelling to indicate the location of the bite. In less than half an hour, however, the characteristic pain appeared, increasing in severity for several hours. It has been vividly described as intense, violent, agonizing, exquisite, excruciating, gripping, cramping, shooting, lancinating, aching and numbing, and was either continuous and incessant or paroxysmal and intermittent. It was felt in the abdomen and generally also in the legs, back, chest, and "all over," less often in the head, shoulders and arms. The pain spreads from the side of the wound by continuity. The final distribution of the pain, disregarding the order of development, however, appears to be fairly uniform, irrespective of the site of the initial lesion, and the pain in the abdomen and legs follows bites of the wrist or back just as regularly as it does those of the penis or ankle.

In addition to the acute pain many other symptoms were described. The most common, in the order of frequency, include profuse cold sweats, restlessness, anxiety, difficulty in breathing, anorexia, nausea and vomiting, constipation, cyanosis, delirium, prostration, shock, insomnia, speech disturbances and acute urinary retention. Tremors, twitching, paralyses, convulsions, localized swelling of the bitten part, or of other tissues, chills, dizziness, priapism, jaundice and a macular skin eruption were also encountered.

An extreme boardlike rigidity of the abdomen was the most striking physical observation, but abdominal tenderness was rarely mentioned. Circulatory disturbances, evidenced by cyanosis and an unduly slow or rapid pulse, were often noted, but actual figures were lacking. Although patients were usually seen by a physician within a few hours after the bite, diagnosis was not always made at once. A few of the patients were operated on for appendicitis and other abdominal disease, while biliary or renal colic, acute pancreatitis, ruptured gastric ulcer and various forms of poisoning were suggested in others. The most acute symptoms lasted a number of hours, no relief being felt for more than six hours in half the cases reported. The pain then generally subsided in from twelve to forty-eight hours after the onset, but complete ease was not secured often for more than a week, and many patients complained of weakness and recurring pains for many weeks thereafter.

While the treatments have been legion, the best results obtained in the last few cases by the Los Angeles Hospital for the last six months followed the use of the convalescent serum; 20 cc. of blood taken from a patient was given intramuscularly. Only four patients have been so treated up to the present time, but in each of these the relief was felt within a few hours after the injection, a comparatively much shorter time than was expected.

An experiment on a young male white rat was conducted. The rat was bitten by a female *Latrodectus mactans*, and the constant characteristic symptoms seem to have been produced by the bite. The author concludes that the series of cases occurring in the Massachussets General Hospital together with the

experimental evidence were sufficient to warrant acceptance of arachnidism, or poisoning from a spider bite as a true clinical entity.

LOEBER, New Orleans.

EXOPHTHALMIC GOITER IN CHILDHOOD. HENRY F. HELMHOLZ, J. A. M. A. **87**:157 (July 17) 1926.

Thirty cases of exophthalmic goiter occurring in children less than 15 years old were reviewed. Administration three times a day of from 5 to 10 minims of compound solution of iodine reduced the basal metabolic rates and toxic symptoms markedly, making preliminary operations unnecessary in the last eleven patients of the twenty-four operated on. Two died, one in crisis twenty-four hours after operation, and the other of bronchopneumonia one week after operation. The fact that the symptoms had been present for from six months to eight years indicates that frequently this disease is overlooked or its seriousness not appreciated. Tachycardia was noted in 100 per cent of the cases, and the thyroid gland was definitely enlarged in all but two. All but two of the patients complained of nervousness. Emotional instability was perhaps the most marked feature. Exophthalmos was definite in twenty-five of the thirty cases, and in one of the remaining five there was the characteristic stare.

BONAR, Salt Lake City.

THE TREATMENT OF ENURESIS. ARTHUR K. BLAU, M. J. & Rec. **124**:492 (Oct. 20) 1926.

Blau, from his observations in a series of cases of enuresis, believes that there is a vesicular atony, particularly of the sphincter, and that underlying this atony is a neurosis, the result of an undeveloped or unstable nervous system. All the causative factors mentioned in the textbooks are contributory factors further undermining this neurotic element. These forms of enuresis may be designated essential enuresis in contradistinction to the few in which the causative factor can be established definitely. Seventy-five per cent of the patients in this series were treated with solution of pituitary given hypodermically and pituitary administered orally. All were improved or cured.

ENURESIS WITH REPORT OF TWO INTERESTING CASES. WILLIAM J. EZICKSON, M. J. & Rec. **124**:493 (Oct. 20) 1926.

Any child who has incontinence during the waking hours after the third year and during sleep after the fourth year should have a thorough physical examination. One must bear in mind the possibility of congenital deformities and abnormalities and peripheral causes acting through reflex irritation.

Culture from urine in one case reported revealed a pure growth of *B. coli*, for which an autogenous vaccine was made. The patient received this vaccine every other day in ascending doses. At the end of two months, the patient was completely cured.

The other case reported showed by roentgen-ray examination the presence of a spinal bifida occulta involving the upper two segments of the sacrum. The family left the city before any treatment had been given.

THE PRESENT STATUS OF OUR KNOWLEDGE CONCERNING THE THYMUS GLAND. I. A. ABT, M. J. & Rec. **124**:525 (Nov. 3) 1926.

It is doubtful whether the thymus is the source of an internal secretion. Probably it supplies the excess of nucleins which the body requires during

the period of accelerated growth. The gland is not considered a superfluous organ. On the other hand, extirpation of the gland in the dog does not influence growth or development, nor does it seem to produce alteration in other organs of internal secretion. A certain number of observers still maintain that there seems to be a relation between the thymus and the sex glands. Exophthalmic goiter at times may produce thymic hyperplasia. The thymus participates in a variety of diseases. It reaches its greatest weight from the eleventh to the fifteenth year, then gradually atrophies, though remnants in most cases continue throughout life. A large thymus may cause dyspnea in young children.

Status lymphaticus is a condition in which there is hyperplasia of the lymphatic tissues and thymus, a small heart and narrow vessels. Such persons are subject to sudden death.

The treatment of enlarged thymus consists of the use of the roentgen-ray or radium.

WILLIAMSON, New Orleans.

ABDOMINAL PAIN IN CHILDREN IN EXTRA-ABDOMINAL CONDITIONS. ALTON GOLDBLOOM, Canad. M. A. J. **16**:1223, 1926.

The author emphasizes the frequency with which abdominal pain is the outstanding feature in cases of infection of the upper respiratory tract. He divides these cases into two groups, the first group showing the pain at the onset of the throat infection but in which the pain subsides in from twenty-four to thirty-six hours, and the second group in which the pain, associated with abdominal tenderness, comes on after the acute infection of the throat. He believes the latter may be cases of adenitis of the mesenteric glands such as were described by Dr. Brennemann.

Four cases of pain in the abdomen associated with intrathoracic disease are reported.

Several hypotheses are advanced to explain the occurrence of the abdominal pain in these cases, but the author states that these are offered only as hypotheses and that more observation is necessary for a true explanation to be given.

The reviewer has noted this symptom in a large majority of cases of tonsillitis, acute nasopharyngeal infections and otitis media during the present epidemic. The association of vomiting and increased peristalsis shown by frequent bowel movements would seem to point toward toxemia as an important etiologic agent. This is the third possibility mentioned by Dr. Goldbloom in his hypotheses.

MOORE, Omaha.

THE ACTION OF EPINEPHRINE IN APLASTIC ANEMIA. ALEXANDER GEORGE GIBSON, Lancet **211**:948 (Nov. 6) 1926.

The story is given of a girl, aged 11 years, who made an apparent recovery from a severe grade of aplastic anemia. Various forms of drug therapy together with seven transfusions of citrated blood were given with only transient halting in the general downward trend. The beginning of recovery coincided with the giving of daily injections of epinephrine (Parke Davis & Co., 1:1,000 solution) beginning with 2 minims and increasing gradually to 5 minims. When the case was reported, the leukocytes, red blood cells and hemoglobin were still below normal. The author ascribes the apparent recovery to probable direct stimulation of the epinephrine on the bone marrow of which some still remained to be stimulated.

LANGMANN, New York.

FIBRO-GÉODIC-OSTEITIS. RECKLINGHAUSEN'S DISEASE OF THE BONE. CHAUVEAU, J. ann. d'anat. pathol. et d'anat. méd.-chir. **3**:243 (March) 1926.

By "maladie osseuse de Recklinghausen's" Chauveau means a disease characterized by a fibrous transformation of the bone marrow. This process leads finally to a dissolution of the medullary tissue with the formation of cavities (géodes). The bone itself undergoes rarefaction. Spontaneous fractures in these cases, followed by deformities and functional disturbances, are frequent. The article is a comprehensive review with a rich bibliography on the subject.

B. M. FRIED.

THE KOTTMANN REACTION IN CHILDREN WITH THYROID DYSFUNCTIONS, NEUROSES AND PSYCHOSES. G. MATTEI, Clin. pediat. **8**:280 (May) 1926.

The Kottmann reaction was studied in seventy children suffering from endocrine disturbances, neuroses and psychotic states. Its behavior showed a wide variation. In the cases of thyroid dysfunctions it varied only a little, and idiots and cerebroplegic and epileptic patients showed a marked retardation. These results agree with those originally obtained by Kottmann. The viscosity of the blood serum, independent of the effects of altered metabolism, plays a large part in the production of the reaction.

ZAMBARANO, Northville, Mich.

DIAGNOSTIC VALUE OF THE BLOOD PICTURE IN THE SO-CALLED SPLENIC ANEMIA OF INFANCY. SILVIA GANDOLFO, Riv. di clin. pediat. **24**:661, 1926.

The author has studied the blood in a child of 11 months with infantile splenic anemia. Hematologically, infantile leishmaniosis and splenic anemia form a definite group and are therefore easily recognized. Splenic anemia should fall into the category of a primary disease and should not be regarded as an anemia secondary to a chronic toxic infection. There is a definite lesion of the bone marrow (myelosis) as both the erythropoietic and leukopoietic functions are disturbed; the changes in the former are most marked.

STUDY OF "FAVISM" IN INFANTS. G. MACCIOTTA, Riv. di clin. Pediat. **24**:721, 1926.

The author describes minutely a disease common in Sardinia, known as "favism"; it is believed to be caused by the bean (fava) — either from smelling the flower or from eating the bean itself.

The disease is characterized by jaundice, hemoglobinuria, acute anemia and transitory nervous and gastro-intestinal symptoms. It is much more severe in children than in adults, being fatal in perhaps 10 per cent of cases.

Chemical studies of the blood in this disease show an increase in the sugar, a diminution in the calcium, magnesium and cholesterin in a normal quantity of sodium and potassium. The serum in vitro is nonhemolytic, while the fragility of the red blood cells is normal or lessened. Morphologically, the red cells may fall in number to 1,000,000 per cubic millimeter; some red cells are nucleated, or show a filamentous network on staining. There is an increase in the number of white blood cells, mostly lymphocytes; in the severer forms, the small lymphocytes predominate, and in the milder ones, the large lymphocytes predominate. Large basophilic mononuclear cells (Turk's or Rieder's cells) are present also. An eosinophilia occurs occasionally.

The author believes that the disease is probably anaphylactic in nature; there seems to be also a familial factor; possibly the allergy is transmitted to the child in utero.

Malaria seems to be a predisposing factor in the development of the disease, while syphilis and tuberculosis are not.

The author obtained excellent therapeutic results by the use of horse serum subcutaneously.

HIGGINS, Cincinnati.

RELAXATION OF THE DIAPHRAGM IN LATE CHILDHOOD. P. FRICK, Monatschr. f. Kinderh. **33**:493, 1926.

Frick reports a case with a description of the roentgen-ray and fluoroscopic examinations. He believes that such cases are not at all uncommon.

GERSTLEY, Chicago.

CONGENITAL STENOSIS OF ESOPHAGUS AND PYLORUS. A. KROKIEWICZ, Vichows Arch. f. path. Anat. **259**:761, 1926.

This is a report of a case of congenital stenosis of the lower orifice of the esophagus and of the pylorus associated with marked distention of the lower portion of the esophagus and of the stomach. The patient was a youth, aged 18.

O. T. SCHULTZ.

THE CONTINUATION OF THE FETAL COURSE OF THE EXCITATION WAVE IN THE HEART DURING CHILDHOOD AND LATER. L. DOXIADES, Ztschr. f. Kinderh. **41**:24, 1926.

The characteristics of the electrocardiogram taken of the newly born baby before his first breath, showing conditions that must be similar to those of the fetus, are an absence of the P and T waves and a strong deflection downward of the R wave. The P and T waves appear after the first breath. The author therefore, considers a well marked S wave, seen in childhood and later, a persistent characteristic of a fetal heart. It is seen in some types of congenital heart disease such as septal defects and patent ductus arteriosis, narrowing of the aorta, as well as in asthenic and nervous hearts and is of great practical importance in small, not infantile, hearts. These hearts are small only because they are less filled with blood in the upright position and are normal in size when the child is lying down. The situation is just the opposite in the liver, an organ which has considerable importance in the circulation because it is innervated from two sources like the heart and because its circulation is markedly changed after birth. In the fetal heart, there is scarcely any difference in pressure between the two sides, and the principal characteristic is a balancing of the blood quantity in diastole. There is less need for a fully developed large heart since the oxygen supply is taken care of by the mother. One may assume, then, that in the fetus and even in adults with small hearts the body is partly dependent on venous pressure in the liver.

A RARE SYNDROME (SOFT AREAS IN THE SKULL, EXOPHTHALMOS, DYSTROPHY—ADIPOSO GENITALIS, DIABETES INSIPIDUS). R. KYRKLUND, Ztschr. f. Kinderh. **41**:56, 1926.

A girl with normal development up to the age of 4 years, with the exception of conjectural pleuritis and pulmonary tuberculosis at the age of 2 or 3, became ill with symptoms pointing to a diabetes insipidus. At 7 years, she showed

beginning dystrophia adiposo genitalis and at the same time a marked exopththalmos. Gradually her head and feet became painful and the fat tissue over the whole body sensitive to pressure. Unevennesses with soft centers were found on the skull. From the beginning of this illness there was a retardation of development, physical and mental, but after treatment with solution of pituitary the pains diminished, there was less restlessness and mental life was more active. Death occurred suddenly in the hospital. Autopsy showed traces of a healed pulmonary tuberculosis and, histologically, tumors resembling sarcoma in the dura, in the brain stem in the region of the hypophysis, in the bones of the skull and in one kidney. There was no change in the hypophysis itself. Only six cases similar to this have been reported in the literature. The primary cause of this complex lay in the sarcoma-like tumor found in different places in the body, and all of the signs such as dwarfism, adiposo genitalis and diabetes insipidus, which are dependent on the disturbance of the inner secretion of the hypophysis, were secondary in this case to the tumor which lay in the brain stem near the hypophysis and interfered with its growth.

HEPATIC INFANTILISM? M. PFLAUNDLER, Ztschr. f. Kinderh. **41**:78, 1926.

An interesting case is that of a boy who showed retarded physical and much less marked mental development. It is difficult to classify the case with any known type of infantilism, since the picture is so dissociated; that is to say, the body length corresponded to that of a child, aged 7; the nutrition to that of 6 years, the length of the lower extremities to that of 5 years, the relative height of the head to that of 4 years, and the calcification of the bones of the wrist to that of a late 3 years. The case might be looked on as a partial form of endocrine disturbance. The early history of the boy was known from stays in various hospitals for contagious diseases from the age of 1 year. His bones were normal at first, and there were no signs of rickets at the age of 2. The case does not correspond to any of Czerny's three types of late rickets. The roentgenograms were examined by Wimberger. The case showed a disturbance of proportion, growth and ossification of distinct type, and with it there was an increase in the size, consistency and function of the liver. This combination has never been described before. Whether an intrathoracic tuberculosis of a mild course was responsible must remain uncertain. The case affords an example of the relation between retardation of ossification and disturbance of function of the liver in childhood.

THE WHITE BLOOD CORPUSCLES IN PREMATURE BABIES, INFANTS AND SMALL CHILDREN: 1. THE NORMAL WHITE BLOOD PICTURE IN PREMATURE BABIES AND INFANTS. S. SCHMAL, W. SCHMIDT and J. SEREBRIJSKI, Ztschr. f. Kinderh. **41**:102, 1926.

The author favors the use of Schilling's formula instead of that of Arneth's: myelocytes; young forms; rod shaped nuecli; segmented nuclei.

This has its disadvantages, but with it in a six to ten minute count of 200 cells an accurate estimate can be made of qualitative changes in the white cells. It is helpful in diagnosis and prognosis but must be used with other data. More work should be done on the scheme, and in its present stage more than one examination of the blood is wise. The observations in infants in this paper were founded on 1,400 blood pictures. The normal white cell count of premature infants is from 10,000 to 20,000 and is reached in the course of a week. In the first twenty-four hours the figures vary from 6,300 to 22,400. The smaller the weight, the stronger the shift to the left. There is no regular birth

leukocytosis in premature infants. Often there may be a leukocytosis which fades in forty-eight hours and becomes normal in the course of a week, but there are cases showing a leukopenia to begin with followed by a leukocytosis and finally a normal count. During the first eight days, there is no "normal white count" qualitatively, but in all cases a shifting occurs which may reach the myelocytes. After the first eight days, the figures in premature babies are: lymphocytes, 45 (75 per cent); segmented nuclei, 15 (40 per cent); rod shaped nuclei, 2 (6 per cent); eosinophils, 0.5 (5 per cent); monocytes, 2 (10 per cent).

In full term infants, at birth the total white cell count varies in the first week between 8,000 and 20,000. In older infants the normal count is from 8,000 to 15,000. Immediately after birth, one observes a high neutrophilic count which often changes after a few days, as a rule, at the end of the first week, suddenly to a lymphocytosis typical of older infants.

The normal differential count for young and older infants is: basophils, 0 (1 per cent); eosinophils, + (5 per cent); myelocytes, 0; young forms, 0 (0.5 per cent); rod shaped nuclei, 0 (6 per cent); neutrophils, 12 (45 per cent); lymphocytes, 45 (78 per cent); monocytes, 2 (12 per cent).

Since in the new-born there are no myelocytes within the first forty-eight hours and since young forms occur only to a limited extent (5.5 per cent in this experiment), it is possible to draw diagnostic conclusions in the first forty-eight hours from a shifting in the leukocyte picture which may reach as far as the myelocytes; that is, it may show a high value for the young forms. There is no difference in the blood picture in breast-fed children as distinguished from bottle-fed children.

WHITE BLOOD CORPUSCLES IN PREMATURE BABIES, INFANTS AND SMALL CHILDREN: 2. THE PATHOLOGIC BLOOD PICTURE IN INFANTS AND SMALL CHILDREN. S. SCHMAL, W. SCHMIDT and J. SEREBRIJSKI, Ztschr. f. Kinderh. **41**:128, 1926.

Mild dystrophy shows normal quantitative conditions but usually a high normal. Severe dystrophy (atrophy) often is accompanied by a leukocytosis and a shifting to the left without any infection being demonstrable clinically. With severe decomposition there is, as a rule, an increase in the neutrophilic cells and a shifting to the left, which is explained by the influence of the decomposition products of the protein from the intermediate metabolism on the marrow system. These observations in atrophy have a certain clinical value for, if a stimulation of the marrow apparatus is present, especially if there is no fever and no objective characteristics, there is a danger in delay.

*Diarrhea.*—In severe diarrheas and intoxications without infection, stimulation of the marrow system is noticeable, but the changes in the blood picture and the severity of the toxic symptoms necessarily do not run parallel since pure alimentary diarrhea may lead to a marked marrow reaction and since infectious dystrophy may lead to the same changes in the blood picture, no conclusion can be drawn as to the alimentary or infectious causation. The small intestine represents the most important absorptive division of the gastro-intestinal canal, and it is to be expected that in the case of injury here changes will occur in the blood picture which do not occur in disease of the same grade in the large intestine. In connection with other clinical examinations, the blood picture may permit a conclusion to be drawn as to the involvement or noninvolvement of the small intestine. As to the prognosis of a diarrhea, many times the blood picture is helpful. Mild diarrhea as a rule shows a mild leukocytosis with some shifting to the left. The changes subside preliminary

to improvement in the stools. Parenteral dystrophy shows a blood picture that is dependent on an infection as a basis. Severe diarrhea usually has a leukocytosis with a predominance of neutrophilic cells and a shifting to the left. Pure alimentary diarrhea leads in many cases to an increase of neutrophilic cells, to a leukocytosis and a shifting to the left. In most cases no conclusion can be drawn as to the causation and the localizatoin of this disease.

*Upper Respiratory Diseases.*—Commonly, there is a small increase in the number of white cells and a shifting to the left. The more severe the infection the higher the fever, and the younger the child, the more marked is the shifting. There is seldom an increase in neutrophilic cells, usually a lymphocytosis.

*Bronchopneumonia.*—No conclusions can be drawn from the degree of leukocytosis as to the prognosis.

*Croupous Pneumonia.*—The smaller the total number of leukocytes the higher the relative value of lymphocytes will be; also, the more shifting to the left.

*Pertussis.*—The average white cell count is from 25,000 to 30,000. An increase of neutrophilic cells instead of a lymphocytosis may occur. In uncomplicated cases there is no shifting to the left. A leukocytosis with relative lymphocytosis is the most frequent picture, but absence of lymphocytes does not speak against whooping cough.

*Tuberculosis.*—As a rule, there is a normal but slight increase in white cells. It is difficult to see whether a relative lymphocytosis exists in infancy, because a lymphocytosis is present normally. Tuberculosis shows a shifting to the left, but this seldom occurs in inactive cases, especially in older children.

*Pus Infections and Sepsis.*—Some cases of sepsis show a low cell count, and therefore the blood count is not a perfect basis for deciding whether to operate or not. A strong shifting is not constant. The changes in the qualitative blood picture within the neutrophilic cells do not depend on the number of cells.

*Typhus.*—There is a leukopenia, a relative lymphocytosis, an absence of eosinophilic cells and decided signs of degeneration in the neutrophilic cells. The blood picture is helpful in the diagnosis of this disease, since often no specific symptoms appear clinically and the disease may progress with the picture of an entirely different disease.

EMERSON, Boston.

PATHOGENESIS OF HEMOLYTIC JAUNDICE. EMIL ZEMAN, Čas. lék. česk. **64**:916 (June) 1925.

The author cites the different theories of hemolytic icterus: hepatogenic, congenital fragility of the red cells, spodogenous splenomegalic, debility of erythroblastic organs, splenohemolytic, hepatosplenic hemolysis and a dysfunction of the reticulo-endothelial organs or structures. Blocking of the reticulated endothelial structures in rabbits with colloidal silver produced a decrease in the hemolysin output. The use of colloidal iron in white rats was unsatisfactory. The function of the spleen seems to be twofold; that is, spodogenous in the absorption of red cells with decreased resistance and instrumental in the development of icterus, judging from the results of splenectomy. The author feels that the spleen and the reticulo-endothelial structures play the chief rôle in the pathogenesis.

CONGENITAL PANCREATIC DEFECT WITH DIABETES MELLITUS. JAN SANETRIK, Čas. lék. česk. **64**:1069 (July) 1925.

The autopsy of a man, aged 43, who had had diabetes with diabetic polyneuritis, myocarditis and generalized edema, showed an aplastic pancreas. This

was irregular, about 4 cm. long, 6 cm. wide and from 0.5 to 3 cm. thick. It had the consistency of a normal pancreas but had practically no islands of Langerhans. This fragmentary organ was apparently sufficient to carry on its work until overcome by an inflammatory and necrotic reaction resulting from chronic alcoholism.

STULIK, Chicago.

SUBACUTE YELLOW ATROPHY OF THE LIVER OCCURRING IN EPIDEMIC JAUNDICE. C. W. HERLITZ and S. NORLEN, Acta Pædiat. **6**:87, 1926.

The authors' case was the only fatal one occurring in an epidemic of twenty cases of jaundice in a small locality. The course of the disease was similar in all cases: lassitude for a few days, then vomiting and diarrhea with the development of mild icterus which lasted about eight days. There was usually bile pigment in the urine, but the stools were normal in color.

The patient, in addition to these symptoms, developed an intense jaundice and died of intestinal hemorrhages on the ninth day. The liver decreased in size, but until the end was able to excrete dyes far better than the livers in other patients who recovered.

With the exception of internal hemorrhages and icterus, the pathologic observations were confined to the liver. A marked necrosis of liver cells with fatty degeneration was found in the peripheral portions of the lobules. Some evidence of regeneration of liver cells from bile capillaries was present, and a marked infiltration of round cells and plasma cells was found in the affected areas.

The authors discuss at some length the causation of such conditions and conclude that some unknown toxic agent is responsible, probably a severe form of the same process that leads to cirrhosis of the liver.

HOLT, Baltimore.

INCREASING FREQUENCY OF CATARRHAL ICTERUS (HEPATITIS EPIDEMICA) AND YELLOW ATROPHY OF THE LIVER IN RECENT YEARS. AXEL THISTED, Ugesk. f. Læger **36**:823, 1926.

Data from different clinical centers show an increase of from 0.4 per cent to 1.4 per cent of catarrhal jaundice and a constant increase in the incidence of acute yellow atrophy over a period of years.

The incubation period of catarrhal jaundice as determined by Lindstedt is from two to four weeks. The disease is contagious during the incubation period and appears to confer lasting immunity.

The question is raised by the author as to whether these two diseases have not a common causation, the acute yellow atrophy being a more severe and fatal form.

SCHLUTZ, Minneapolis.

## Nervous Diseases

FAMILIAL PREADOLESCENT MENTAL DETERIORATION AND BLINDNESS. TAFT and MONROE, Am. J. Psychiat. **5**:87 (July) 1925.

The histology of one case is given. These authors agree with Sachs that there "is danger in entering on further speculation regarding the hereditary factors of this disease. As a result of recent biological instruction, I think a little less of heredity, per se, and a little more of the influence of environment and extraneous agents on the ovum during the period of development."

MENTAL DISORDERS OF CHILDHOOD. C. W. BURR, Am. J. Psychiat. **5**:145 (July) 1925.

Burr limits his discussion to children who are normal until "later childhood, puberty or adolescence," when they break. He thinks that "more than a few queer children could be guided to healthy maturity," and perhaps some geniuses saved, if more attention were paid to clinical psychology, particularly that of sick children. A number of illustrations are given of mental ailments associated with acute or chronic abnormalities or diseases.

PSYCHOTIC CHILDREN: TREATMENT AND PROPHYLAXIS. A. A. BRILL, Am. J. Psychiat. **5**:357 (Jan.) 1926.

Brill has followed the development of a number of psychotic children into adult life, in order to study the reaction types, and to draw "conclusions, speculative perhaps, concerning treatment and prophylaxis." This unnumbered group was predominantly schizoid or syntonic. In the author's opinion, a stage in psychiatric diagnosis has been reached in which it is safe to speak of "tendencies" as one does in physical diagnosis. The recognition of an exaggerated emotional state in early life "can produce a sort of immunity for subsequent schizoid or syntonic disturbances." Proper management in childhood will sometimes forestall an emotional or mental breakdown later. "Ideal prevention in such cases must start with the parents; they should know how to manage their children. . . . But if the schizoid or syntonic mechanisms crop up in sufficient numbers to create disturbances in the average child, the only rational management is through psychanalytic approach."

RESEARCH PROBLEMS IN EPILEPSY. C. E. GIBBS, Am. J. Psychiat. **5**:415 (Jan.) 1926.

Gibbs feels that as an indispensable preliminary to the effective study of epilepsy the ground should be cleared by sifting and sorting the immense mass of fact and opinion that has grown up—and continues to accumulate—about this disease. Suitably arranged, this would serve as a basis for "some coordinated and comprehensive plan for research." Gibbs believes also that a study of epilepsy involving the endocrine glands should be developed from a broad clinical and biologic point of view.

EPILEPTOID REACTIONS IN CHILDREN. V. C. BRANHAM, Am. J. Psychiat. **5**:423 (Jan.) 1926.

The term epileptoid refers to a miscellaneous assortment of manifestations epileptiform in character. These fall into three main groups: (1) the latent type of epilepsy, most frequently nocturnal, in which night cries, somnambulism, inarticulate talking in sleep, and frequent falling out of bed, with dulness and stupidity the next morning, are suggestive symptoms (the periodicity of this picture is of even more importance); (2) the group with features of petit mal and only brief loss of consciousness; (3) a group in whom no demonstrable seizure can be elicited. This is the true epileptoid group, i. e., not really epileptic. Still, even among this group there may be a prodromal aura, dizziness, severe headache, pallor, dilated pupils, and a diffuse myoclonus. The members of this group especially are emotionally unstable; vasomotor disturbances are common, and a moderate degree of mental retardation is usual. It is necessary to practice careful control of the environment and hygiene, with some assistance from drugs, such as whole gland pituitary and phenobarbital.

LYON, Boston.

A Study of Subject Matter and Motivation of Children's Dreams. Phyllis Blanchard, J. Abnorm. Psychol. **21**:24 (April) 1926.

This is a tabulated statement of the physical and mental condition of 189 children who recalled their dreams, the age at which they occurred, and the type of subjects of the dreams. Forty-six per cent were classed as wish fulfilments and 40 per cent were related to fear. It is realized that dreams of children may be of real clinical assistance in coming to an understanding of the child's difficulties and general psychology.

Hamill, Chicago.

The Rôle of the Midbrain in the Pathogenesis of Adiposogenital Dystrophy. E. J. Kraus, Med. Klin. **22**:485, 1926.

Kraus reports the case of a man, aged 36, who, about twenty-two months before death, suffered an injury to the head. He complained of headache and marked nervousness, developed a eunuchoid type of adiposity with pain in the fat deposits and became impotent. Postmortem examination showed a nonspecific type of sclerosing encephalitis limited to the floor of the third ventricle of the brain; the hypophysis was normal except for a slight atrophy of the anterior lobe; the testes were of normal size; spermatogenesis was present and there were few Leydig cells. Kraus is convinced that there is such a close interrelation between the hypophysis and the floor of the third ventricle that a lesion involving one will, in time, extend to the other; he believes that the obesity in this case was associated with the lesion of the brain, and the changes in the genital organs with the atrophy of the anterior lobe of the hypophysis.

J. P. Simonds.

Diagnosis of Cerebellar Tumors in Children. Macdonald Critchley, Brit. J. Child. Dis. **23**:165 (July-Sept.) 1926.

In a previous paper, the author stated that in a series of 125 cases of intracranial tumors in children the neoplasm was situated under the tentorium in 47.2 per cent of the cases. Tumors originating in the cerebellum or pons constitute these subtentorial neoplasms; the former are the more frequent. A large number of tumors belong to the intermediate class, the so-called "pontocerebellar," which may arise primarily in either pons or cerebellum. It is of great practical importance to differentiate between the two types, as the prognosis is so different. Pure cerebellar tumors frequently can be removed in toto, and even when this is impossible decompression effects a great improvement. Tumors of pontile origin are never removable, and there is no improvement after decompression.

*Symptoms in Pontile and Cerebellar Tumors*

| | Tumors Primarily Pontile | Tumors Primarily Cerebellar |
|---|---|---|
| Drowsiness | Occurs early | Occurs late |
| Difficulty in swallowing | May be present | Absent until very late |
| Papilledema | Occurs late or never | Appears early and rapidly becomes intense |
| Cranial nerve palsies | Very early | Late |
| Spasticity (absent abdominal reflexes, exaggerated tendon reflexes, Babinski clonus) | Early | Late |
| Sensory loss | Not uncommon | Rare |

*Microscopic Character of Cerebellar Tumors.*—They are gliomas or tuberculomas; a few are cholesteomatous in nature. A large proportion are partially or wholly cystic.

*The Four Main Symptoms.*—In order of occurrence the symptoms are: (1) vomiting — earliest complaint in 72 per cent; forceful, mainly early in the morning; (2) headache — frequently early, occipital, suboccipital or cervical, later also frontal; aggravated by stooping, coughing, straining or crying; (3) disturbances of equilibration — staggering gait, tremor of limbs at rest or during effort; fine tremor or titubation of head and shoulders; (4) disturbances of vision — blindness and diplopia.

Another symptom occasionally encountered, the so-called "cerebellar fit," consists of generalized tonic rigidity of the entire musculature, there being no premonitory symptoms or aura.

*Physical Signs.*—Those due to actual cerebellar disturbance are: loss or diminution of muscular tonus and upset in fine muscular coordination resulting, variously, in atonia, ataxia, asthenia, dysarthria, papilledema, dysdiadochokinesia, etc. Cerebellar manifestations are ipsolateral in distribution.

Those due to pressure on adjacent structures are: squints and paralyses of other cranial nerves, especially the fifth and seventh; skew-deviation of eyes if Deiter's nucleus is involved; distortion of the pons, which may produce signs of pyramidal involvement; e. g., spasticity, ankle clonus and the Babinski sign.

Those due to generalized hydrocephalus are: enlargement of the cranium with thinning of the skull bones and separation of the sutures, and paralysis of one or both sixth nerves.

EPILOIA. T. BRUSHFIELD and W. WYATT, Brit. J. Child. Dis. **23**:178 (July-Sept.) 1926.

The term "epiloia" is applied to a syndrome of mental deficiency, epileptic fits, adenoma sebaceum, nodular sclerosis of the cerebral cortex and tumors of the kidney and other organs.

This rare condition is generally congenital. Among 2,412 admissions to the Fountain Mental Hospital, the author found sixteen cases of epiloia. The patients varied in age from 2 to 13 years; they were either idiots or imbeciles, and were subject to epileptic fits. The adenoma sebaceum appears about the fourth or fifth year and is first seen in the nasolabial folds on the two sides of the face.

No clinical signs of internal tumors were found in these cases. According to Hyman, kidney tumors are found in 80 per cent of the cases; they are benign and do not give rise to symptoms.

LANGMAN, New York.

MENINGITIS AND PSEUDOMENINGITIS COMPLICATING INTESTINAL TENIASIS. BARRAUD, Arch. de méd. d. enf. **29**:389, 1926.

Professor Arnozan said recently: "Our grandfathers attributed to intestinal worms affections most bizarre and incongruous; our fathers believed they were entirely without pathological significance; our contemporaries, wiser than either, recognize the truth rests somewhere between these extremes."

Since Guillain and Gardin reported before the Academy of Medicine (1922) a case of meningitis which, they maintained, was due to forms, a number of

observations of this character have been published in the French medical press. Long before this, however, the remote possibilities of intestinal infestation were remarked. Lebon, in 1835, reported twenty-nine cases, seen in a period of eight years. In 1844, Mauliere described an invasion in a child of 2, with paralysis of both legs and strabismus. This child promptly recovered after the expulsion of round worms.

Bouchut defined a pseudomeningitis from this source as a neuropathy, characterized by fever, irregularity of the pulse, vomiting, constipation, delirium and headache, due to irritation of the meninges by the toxins of *Ascaris lumbricoides* or of *Oxyuris vermicularis*. The author quotes numerous instances from the voluminous literature on the subject to sustain his contention. From these, as well as from his own experience, he attempts to classify the disorder as follows: (*a*) those cases which clinically resemble meningitis, but in which the cerebrospinal fluid is normal; (*b*) cases in which the clinical manifestations are accompanied by alterations in the cerebrospinal fluid.

His conclusions will not be accepted readily by American clinicians.

ASTHENIA IN INFANTS. BENON, Arch. de méd. d. enf. **29**:525 (Sept.) 1926.

What may be called the nervous and mental pathologic condition of infancy presents neither the wealth nor the variety of types seen in adult life. This is readily explained; the sensations and the emotions of the infant have not yet reached a development in which distinct nervous or psychic diseases may be readily defined. From 25 to 40 years may be called the age of predilection to mental disorders.

*Diagnostic Considerations.*—Asthenia, in an infant, is difficult to appreciate. Cases reported by the author have been followed for as long as twenty-four years without a trace of organic disease being discovered. In the very young one frequently finds asthenic periods or fits of depression of varying degrees. These attacks, whether due to an infection or an intoxication and sometimes obscure but often readily traced, disappear in a few hours or, at most, in a few days. This may be called normal or physiologic asthenia. It is particularly important, however, to differentiate this acquired asthenia from constitutional asthenia, apathy, dementia and mental confusion. By constitutional asthenia one assumes a mental state dating from birth, changing but little in the symptomatology and showing in its evolution few mental or nervous complications. Apathy is unlike asthenia. While the general motor activity of the apathetic patient is reduced, he differs in one important essential from the asthenic patient in that he does not become easily fatigued. Asthenia can be differentiated from dementia only if the intellectual development of the child has reached a stage at which it is possible to make a psychanalysis. In this examination, it is necessary always to include the mediate observation of the parents or other interested persons in order to appraise properly the psychic defect existing. The question often arises whether in infancy there is an extremely precocious dementia. How may one distinguish between acquired idiocy, constitutional asthenia and acquired asthenia? As far as confusional states in early childhood are concerned, they are, as in adult life, more the result of infections and are essentially acute, with lucid or partly lucid intermissions. The treatment centers about prolonged and complete rest, with more than ordinary attention to diet and physical comfort.

AMESSE, Denver.

THE WEIL-KAFKA REACTION IN SOME OF THE DISEASES OF INFANCY. G. TACCONE, Clin. pediat. **8**:385 (July) 1926.

The following results were obtained with the Weil-Kafka reaction:

1. (First Stage) Test for the Total Complement: This was positive in eight cases of tuberculous meningitis with other typical changes in the spinal fluid.

2. (Second Stage) Test for Hemolysins Only: This was positive in one case of Little's disease. The blood Wassermann reaction was positive and the spinal fluid Wassermann reaction negative. The spinal fluid showed also a slight hyperalbuminosis and a moderate lymphocytosis. The fluid gave a positive reaction in two cases of hydrocephalus, one of congenital origin and the other secondary to cerebrospinal meningitis. There were positive globulin and albumin reactions in the spinal fluid.

The test was reported positive in one case of acute lethargic encephalitis in which increased albumin, globulin and a lymphocytosis were found in the spinal fluid. Positive reactions were obtained also in seven cases of anterior poliomyelitis in the paralytic stage. The test for hemolysins was negative in one case of cerebral tuberculoma, in one case of cerebral paralysis of syphilitic origin; two cases of congenital syphilis; one case of congenital hydrocephalus; three cases of lethargic encephalitis (two of these showed parkinsonian changes); eight cases of anterior poliomyelitis; five cases of pneumonia, with signs of meningismus, and two cases of typhoid with meningeal symptoms.

The author concludes that the Weil-Kafka reaction is always negative in normal spinal fluid. A positive reaction is associated with changes in meningeal permeability. When positive for the presence of the total complement, the test is an expression of profound lesions in the meninges. When positive for the hemolysins only, it indicates less serious disease. Although a positive reaction indicates meningeal disease, its negativity does not exclude it. The two steps of the reaction (total complement and hemolysins) do not constitute a means of differential diagnosis between various lesions having the same causation. The prognostic value of the test is limited. Its practical value is of great importance in attempting to determine meningeal integrity in various syndromes, especially in traumatic conditions of the cranium and spinal column.

HYSTERIA IN CHILDHOOD. G. CARBONARA, Clin. pediat. **8**:417 (July) 1926.

Four cases of hysteria in children are reported. The symptoms presented simulated organic diseases of the nervous system. All the patients were cured by psychotherapy.

ZAMBARANO, Northville, Mich.

THE RELATION BETWEEN BERIBERI AND TETANY. GINO FRONTALI, Riv. di clin. pediat. **24**:577, 1926.

Experiments were made on fifteen rats and six pigeons, using (1) a normal ration, (2) a ration deprived of vitamin B, (3) polished rice, and (4) polished rice with bran. The author noticed that the nervous symptoms, when there was lack of vitamin B, were accompanied by a hyperexcitability to galvanic current, and a reduction of calcium content of the blood; this is analogous to the observations in infantile and postoperative tetany.

THE FACIAL PHENOMENA AND THE CALCIUM CONTENT OF THE BLOOD IN CHILDREN. C. LOMBARDI, Riv. di clin. pediat. **24**:649, 1926.

The author found a positive Chvostek sign in 150 of 819 children between 3 and 10 years of age. The calcium content of the blood and the galvanic excitability were determined and found to be normal in twenty-nine children of this age group with a positive Chvostek sign.

HIGGINS, Cincinnati.

PSEUDOHYPERTROPHIC MYOPATHY OF DUCHENNE WITH MANIFESTATIONS OF ENDOCRINE INSUFFICIENCY. LUIS MORQUIO and J. M. ESTAPÉ, Arch. latino-am. de pediat. **20**:566, 1926.

The authors report a case of pseudohypertrophic myopathy of the type of Duchenne. Associated with the primary progressive myopathy was a pluriglandular endocrine insufficiency. The authors regard this endocrine phase as the principal etiologic factor, according to the glandular theory of Claude as against the theory that the principal etiologic factor must be sought in the neuromuscular mechanism.

SCHLUTZ, Minneapolis.

PNEUMOCOCCUS MENINGITIS IN INFANCY. EUGEN STRANSKY and ALEXANDER WITTENBERG, Jahrb. f. Kinderh. **63**:246, 1926.

The authors report five cases of pneumococcic meningitis that they have seen and review the literature. They think that there are two distinct clinical forms: an acute and a chronic type. The first is easy to recognize and gives a hopeless prognosis. The second form, in which the liquor is clear for some time and the pneumococci not easily found, has a longer course and the patient may recover as one of the three patients of this category did. They think that cases of the latter type sometimes are diagnosed as serous meningitis.

SALAAMINGSPASM. MARIA LEDERER, Jahrb. f. Kinderh. **63**:275, 1926.

This condition, known as a sudden spasm imitating the oriental salutation, occurs in idiotic and mostly in microcephalic children. It is a rare condition, but the author observed eleven cases during one year. In six of the eight cases in which encephalography could be done, it showed occult internal hydrocephalus with microcepalus. The author believes with others that this spasm is a subcortical focal epileptic manifestation — "pallidum epilepsy." There was no postmortem examination in any of the cases.

PARMELEE, Chicago.

MYATONIA CONGENITA (OPPENHEIM). EUGEN STRANSKY, Monatschr. f. Kinderh. **34**:24, 1926.

Stransky reports three cases of myatonia congenita. He believes that the presence of contractures in the joints is evidence in favor of the pathologic changes being not muscular weakness and disturbance in muscle development but rather muscle atrophy. He does not wish to state whether the atrophy is spinal in type.

GERSTLEY, Chicago.

DEATH RESULTING FROM PUNCTURE OF THE CISTERNA MAGNA. F. REUTER, Wien. klin. Wchnschr. **39**:1275 (Oct. 28) 1926.

A boy, aged 14, who for five months had had symptoms suggestive of brain tumor, was subjected to puncture of the cisterna magna. As the needle first entered, a small quantity of cerebrospinal fluid was obtained under increased pressure. The flow then ceased and the needle was reintroduced at the same site. Only blood was obtained now; the pulse became weak and cyanosis appeared. In spite of repeated stimulants, death ensued thirty minutes after the first puncture.

At the autopsy, Reuter found premature ossification of the sagittal and lambdoid cranial sutures. There was evidence of increased intracranial pressure: cerebral markings on the inner table of the skull, flattened convolutions, cerebral edema, dilated lateral ventricles, and displacement of the pons, medulla and cerebellum against the foramen magnum. A tumor or encephalitis could not be demonstrated. Hemorrhages existed in the subarachnoid spaces of the pons and cerebellum. A puncture wound led through the medulla to the fourth ventricle, which was filled with blood. This trauma and hemorrhage had evidently been the cause of death.

The author believes that in such cases in which increased intracranial tension exists, the contents of the posterior fossa (cerebellum, pons, medulla) are displaced toward the foramen magnum with resultant partial or complete obliteration of the cisterna magna. If a small amount of fluid is present in the cisterna, its removal may be followed by complete arachnoid block, or the medulla may be pierced easily. In such conditions, which can be foretold clinically by symptoms of irregularity of respiration and pulse, one should be cautious in performing cisterna puncture.

PREMATURE OSSIFICATION OF SKULL. P. LUDEWIG, Wien. klin. Wchnschr. **39**:1308 (Nov. 4) 1926.

Two children with clinical histories of progressive paralysis and convulsions were found at autopsy to have complete synostosis of the principal cranial sutures. A review of the literature disclosed several theories as to the cause of premature synostosis, e. g., primary ossification, circulatory disturbances of the skull and brain following meningitis, encephalitis, or trauma.

Ludewig was convinced that roentgenology offered the most accurate data on premature synostosis of the skull. Under his direction thirty patients from an insane asylum with histories of epileptiform convulsions were examined by the roentgen ray to determine the state of ossification of the principal cranial sutures. Complete obliteration of three principal sutures (coronal, sagittal, lambdoid) was found in six cases, of two sutures in eight cases, and of one suture in three cases. Of the seventeen patients with premature synostosis, eight were syphilitic; four were microcephalic idiots; four had merely a history of convulsions, and one had had a previous purulent meningitis. The author stresses as possible etiologic agents in the production of premature synostosis various inflammatory conditions; e. g., syphilis, circumscribed osteomyelitic foci, healed meningitis or encephalitis with impairment of blood supply, etc. He concludes that congenital syphilis has an important relation to premature cranial ossification while idiopathic epilepsy is much less frequently associated with it.

OLMSTED, Seattle.

CONCERNING THE SUPPOSED ALKALOSIS IN EPILEPSY. F. FRISCH and E. FRIED, Ztschr. f. d. ges. Exper. Med. **49**:462 (April) 1926.

Twenty-three cases are cited in which the $p_H$ only occasionally was above or below normal limits (7.48 and 7.58, according to the Hollo and Weiss technic). From four to twelve determinations were made in each case before and after convulsions, and during quiescent periods. In one case there was a decompensated alkalosis ($p_H$ 7.77 carbonic acid, 62.3 volume percentage) in the middle of a ten day quiescent period. No acidosis followed the convulsions.

Förster has shown that an epileptic seizure may be brought on by hyperventilation. In five epileptic patients hyperventilation did not produce an attack, even with a $p_H$ of 7.75 and a plasma bicarbonate of 53.3 per cent. The authors feel that alkalosis alone is not the precipitating factor of convulsions in epilepsy. They conclude that a disturbance of the acid-base equilibrium, as shown by a shifting of the actual blood reaction, does not occur in epilepsy.

W. B. BRAHDY, New York.

THE TREATMENT OF EPILEPSY. E. FREUDENBERG, Ztschr. f. Kinderh. **41**:46, 1926.

The author reports one case of epilepsy which showed a definite dependence of convulsions on the height of the blood chloride curve and an independence of acid base equilibrium. The convulsions did not occur with a chloride under 0.50. After the administration of bicarbonate and a diet poor in salt (the author has never known, as far as could be made out from the literature, this combination to be used) the chloride curve could be held low for a long time. There are, of course, other cases of epilepsy which react otherwise to a lack of chloride and to alkalosis.

EMERSON, Boston.

## Diseases of the Ear, Nose and Throat

ADENOIDS AND TONSILS IN CHILDHOOD. A PLEA FOR CONSERVATION. A. J. WARING, J. M. A. Georgia **15**:384, 1926.

Waring states that adenoids may have and that the tonsils probably have a definite function. After the obvious cases over which there can be no disagreement are omitted, each case should therefore be studied conjointly by physician and specialist, and the merits of the operation carefully considered. The question of adenoidectomy and tonsillectomy should not be considered conjointly but separately, for the pathologic condition is not always the same; the operative risk is not equal, or the need for excision identical.

Preoperative study of the patient's condition to diminish the risk of fatality is not always comprehensive but it should be.

MASHBURN, Atlanta.

DISTURBANCES OF PRODUCTION OF RHYTHM IN DEAFMUTE CHILDREN. OSKAR BÉNESI, Ztschr. f. Hals-, Nasen- u. Ohrenh. **16**:7 (July 31) 1926.

1. Twenty-four deafmutes, aged from 8 to 15 years, were examined for their ability to reproduce optic, tactile and kinesthetic rhythms.

2. Only six children were able to make approximately correct optic and tactile reproductions. One child gave a false reproduction of tactile rhythm.

3. The optic test gave the poorest results; the tactile gave better results, and the kinesthetic the best.

4. Control experiments on normal and feebleminded children proved that they responded well to the tasks imposed.

5. Among deafmutes who reproduce rhythms, subjects with preserved labyrinth function were in the majority. They also formed the majority in the group of subjects able to reproduce the same rhythms.

6. Such an unequivocal influence of the absence or presence of the cochlear function cannot be shown.

7. The author believes, therefore, that the vestibular nerve plays an important rôle in the physiologic mechanism of voluntary rhythm. The experiments prove that it is probable that the labyrinthian influence on rhythm depends on the otoliths.

CHRONIC OTITIS MEDIA IN 1911-1921, AT THE UNIVERSITY EAR CLINIC IN FRANKFORT ON THE MAIN. STERN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **16**:162 (Sept. 22) 1926.

During the years 1911 to 1921, 5,380 patients suffering from chronic middle ear suppuration (71.3 per cent) were observed, compared with 2,160 patients (28.7 per cent) who suffered from acute middle ear suppuration. In consequence of the war, the number of patients was larger in the years from 1914 to 1919 on account of such factors as injuries to the ear and undernourishment. There were three and one-half times as many male as female patients. Most cases occurred during the second and third decades, while in acute otitis media most cases occurred during childhood. With the exception of infectious diseases, in 3.7 per cent of cases, the cause of chronic otitis media is difficult to establish. It must be assumed from the beginning that the disease will be chronic, although it must be admitted that in the development of mesotympanal disease changes in the nasopharynx play an important rôle. In 0.65 per cent, tuberculosis could be shown; in 59.9 per cent, diseases of the nasopharynx, of the nose and of the nasal accessory cavities were found. Chronic otitis media is classified as mesotympanal in 56 and epitympanal in 27.8 per cent of cases. Both forms were present in 7.8 per cent. In 8.4 per cent, the localization of the perforation was not mentioned. The symptoms were discharge, then headache and pain in the ear, followed by difficulty in hearing. In 54 per cent of the patients sound conduction was impaired and in 6.7 per cent sound perception. Both were impaired in 36.1 per cent. Vestibular hypoexcitability was present in 19.6 per cent, vestibular hyperexcitability in 6.9 per cent. Three and a half per cent reacted differently calorically and after turning. With seven exceptions, leading to a mastoid operation, the mesotympanal middle ear suppuration was treated conservatively. Of the epitympanal cases, eighty-seven patients (18.1 per cent) were treated conservatively; 3,913 (81.9 per cent) were treated surgically — of these, 75.1 per cent underwent radical operations and 24.9 per cent attico-antrotomies. Forty-seven mesotympanal and fifty-one epitympanal suppurations were associated with mastoiditis, which in seven mesotympanal and in all epitympanal cases led to an operation. Thirty-one times a facial paresis was noticed, twenty-one times before and ten times after the operation. In forty patients an extradural abscess was found during the operation. Seventy-five per cent of these were cured. In sixty-one patients, a labyrinthitis developed. Of these thirty-two had a fistula of the semicircular

canal, and of these eighteen had a symptom of fistula. A complete labyrinth operation was performed on eighteen patients, a partial operation on one patient. Six (31.6 per cent) died; thirteen (68.4 per cent) were cured. Of those who had not been operated on, ten (23.8 per cent) died; all others (72.2 per cent) were cured. In six patients a sinus thrombosis was found; five of these patients (83.3 per cent) died of further ear complications. Seven abscesses of the brain were observed, four of the cerebrum and three of the cerebellum. Three patients suffering from abscesses of the brain died. In seven patients, a meningitis serosa was present. These patients recovered. In sixteen patients, a suppuration meningitis was found. Six of these patients, 37.5 per cent, recovered. In all, twenty-three patients died, seventeen of whom, 0.31 per cent, died on account of a disease of the ear.

AMBERG, Detroit.

## Diseases of the Skin

DERMATITIS OF THE BUTTOCK. A. B. MARFAN, Nourrisson **14**:65 (March) 1926.

In breast-fed infants, one often encounters a dermatitis characterized by a marked erythema which is kept moist by a persistent exudation. This erythema, when associated with a seborrheic eczema of the scalp and face, may progress to the erythrodermia desquamativa of Leiner. The duration is from three weeks to two months; the condition is often serious in its clinical picture and may even go on to a fatal outcome. A streptococcic infection has been held responsible as the etiologic factor, but actual proof is wanting.

The vesicular type of dermatitis is more benign in its manifestations and more amenable to treatment. The vesicles come and go quickly, papules may follow or superficial ulcerations may appear.

Both types of eruption are due to, or at least are aggravated by, the irritation of the urine. In treating the vesicular type, Marfan prefers a sterile ointment composed of equal parts of hydrous wool fat and petrolatum. The erythematous type is less tractable, but as it appears exclusively in breast-fed infants, the author advises the institution of a mixed feeding regimen in all these infants.

THE WHEAL TEST. L. RIBADEAU-DUMAS AND MLLE. TISSERAUD, Nourrisson **14**:79 (March) 1926.

This work was suggested by that of McClure and Aldrich, in 1923, when they reported on the time of absorption of intradermal injections of normal saline solution, especially in cases of nephritic edema. Ribadeau-Dumas and Tisseraud conducted their tests with Ringer's solution, glucose solution, dilute horse serum and antipneumococcic serum. In normal infants the absorption time was found to be about an hour. This was prolonged in cases of athrepsia, showing that these patients in spite of extreme emaciation are not actually suffering from any marked loss of water. On the contrary, the absorption time is markedly shortened in premature infants and in cases of marked diarrhea, proving the necessity of administering fluids by all available routes to these patients. Saline and glucose solutions are rapidly excreted in the urine. The serums should be retained longer and additional studies should be made to determine which ones can be administered safely and the proper dilution for them.

MCCLELLAND, Cleveland.

PERSPIRATION IN THE INFANT. JEAN MEYER, Rev. franç. de Pédiat. **1**:409 (Oct.) 1925.

This article calls attention to the experimental and clinical possibilities entailed in a consideration of the amount of water lost by perspiration. Studies were made according to a loss in weight for determining the method of the cutaneopulmonary perspiration; this was computed in grams per kilogram of body weight, and grams per square decimeter of surface area. The latter was found to be a constant factor in normal persons and amounts to 0.4 Gm. per square decimeter per hour at 18 C.

The studies made on sick infants showed the following facts: In diarrheas with dehydration, the great increase in loss of water seemed to be due to excessive perspiration, the diarrhea itself only compensating in amount for the concomitant suppression of urine. In the infants without dehydration, the amount of perspiration was small. In acute inanition the decrease in perspiration parallels the lowering in metabolism; in chronic inanition it is normal. In fevers, with the rise in temperature there is a diminution in perspiration and with the fall there is an increase. When the temperature is stable, the production of heat and perspiration varies in different conditions. Three types were found: (1) a banal type in which the perspiration was a little increased; (2) a type showing retention of water with edema without oliguria, in which the perspiration is very feeble, and (3) cases with dehydration and excessive perspiration. In death with hyperpyrexia, there is considerable production of carbon dioxide and little perspiration. In death with hypopyrexia, there is little production of carbon dioxide with excessive perspiration.

LESLIE, Chicago.

CHANGES IN THE SERUM REFRACTION IN ERYTHRODERMIA. E. SCHIFF and W. BAYER, Monatschr. f. Kinderh. **34**:17, 1926.

In the beginning of a case of erythrodermia desquamativa, the protein concentration in the blood serum is normal or at any rate is only slightly diminished. During the height of the disease, the protein diminishes noticeably and returns to normal with recovery. Only in cases associated with severe loss of water does the protein concentration rise. On the other hand the decrease in protein is not due to a hydremia, for though blood water is increased, it is not in proportion to the decrease in protein. Erythrocyte counts also confirm this observation.

The authors offer the theory that the decrease in protein is due to a transfer of the serum protein to the tissues.

This diminution in serum protein may be of diagnostic value in differential diagnosis and is also an aid in prognosis. As long as the protein is below normal, the child is not out of danger.

GERSTLEY, Chicago.

TREATMENT OF ECZEMA WITH INTRAVENOUS INJECTIONS OF TEN PER CENT SOLUTION OF SODIUM CHLORIDE. J. SELLEI, T. BARSONY and E. LIEBENER, Orvosi hetil. **70**:465, 1926.

Daily injections of 10 per cent sodium chloride solution have had good effect in the treatment of eczema and dermatitis. The acute process improved cervical glands, 33 per cent. No routine study of the nasal accessory sinuses

rapidly. The subacute processes showed a less rapid improvement. Similar results have been obtained with 10 per cent sodium bromide solution. The treatment is without any untoward effects.

ZENTAY, St. Louis.

## Surgery and Orthopedics

SPINAL ANESTHESIA IN INTUSSUSCEPTION OF INFANTS. HAMILTON BAILEY, Lancet **111**:648 (Sept. 25) 1926.

The standard dose (9.2 cc.) of stovaine in saline solution should be used, but this must vary with the weight of the baby. The cerebrospinal fluid should not be allowed to escape; 0.5 cc. of solution of pituitary should be injected subcutaneously to counteract the fall in blood pressure.

The advantages of this type of anesthesia are that it is effectual, rapid and within reasonable limits there is no particular necessity for speed, and furthermore it gives an absolutely relaxed abdomen. The author recounts one fatality attributable, he believes, to an overdose of stovaine.

LANGMAN, New York.

ACUTE OSTEOMYELITIS OF THE MAXILLA IN INFANTS. TESAR-VACLAV, Čas. lék. česk. **64**:921 (June) 1925.

The site of osteomyelitis, according to frequency, is given as tibia, femur, humerus, cranial plates, mandible, terminal phalanges, maxilla, pelvis, sternum and ribs. The differential diagnosis of necrosis of the maxilla includes sequelae of dental caries, tuberculosis and syphilis, the necrosis following phosphorus poisoning and infectious fevers and the idiopathic group. Because of the similarity of observations, this condition is often reported as an empyema of the antrum of Highmore. The ages of the infants cited were 6 weeks and 7 months, and both made an uneventful recovery after the removal of sequestrums and infected tooth buds.

STULIK, Chicago.

ACUTE INVAGINATION OF THE INTESTINE IN SMALL CHILDREN. S. MONRAD, Acta Pædiat. **6**:31, 1926.

This report deals largely with the author's method of bloodless reduction by "taxis"—or manual manipulation through the abdominal wall under anesthesia. The details of the procedure are well described. In a series of about 100 cases, more than 80 per cent yielded to this form of treatment alone, with a mortality of only 14 per cent. The author does not, however, recommend this method for all cases. The ileocecal and the colic forms of intussusception are more easily reduced than the iliac and ileocolic. When there is reason to believe that one of the latter forms is present, when the invagination has lasted a long time, and when the child is over 2 years of age, he feels that primary laparotomy is preferable.

HOLT, Baltimore.

## Miscellaneous

THE INCIDENCE OF PHYSICAL DEFECTS AND NON-TUBERCULOUS DISEASE AMONG TWO THOUSAND CHILDREN EXAMINED FOR TUBERCULOSIS. EDMOND NELSON and J. A. MYERS, Am. Rev. Tuberc. **14**:448 (Oct.) 1926.

The oustanding physical defects in this group were carious teeth (17 per cent), malnutrition (26 per cent), enlarged tonsils (29 per cent) and enlarged

was made, but from their experience the authors are convinced that in obscure cases roentgenograms of the sinuses are almost as important as roentgenograms of the chest.

Because of the many difficulties in differentiating mild tuberculous disease and many nontuberculous conditions and the tremendous responsibility a decision implies, diagnosis always should be withheld in doubtful cases until detailed examinations, a satisfactory period of observation and careful analysis are possible.

SMITH, Ogden, Utah.

MUNICIPAL CHILDREN'S POLICE OF AMSTERDAM. HOGENDYK, Rev. internat. de l'enf. **2**:777 (Sept.) 1926.

The establishment of a coordinate branch of the police service, operating exclusively among children, and its progress since 1920 are discussed by the commissioner in charge. Covering practically the same ground as do our own juvenile courts, the objects of the bureau are set forth under the follow-subdivisions:

1. To aid in the most effective manner possible those parents who have reported improper conduct of their children.

2. To prevent grave negligence in the care and education of children.

3. To assist public institutions in finding suitable homes for waifs and foundlings.

4. To aid school superintendents in the problems of truancy.

5. To furnish evidence for the courts in all cases, civil and criminal, involving children.

6. To exercise surveillance over children at play in public places and particularly to have jurisdiction over beggars, street singers, juvenile acrobats and the like.

The motto of the corps "Prevention is better than cure" seems to have been ably exemplified in its operations thus far.

CORRELATING CORRECTION FOR CRIPPLED CHILDREN. SINCLAIR, Rev. internat. de l'enf. **2**:789 (Sept.) 1926.

This article is a brief survey of the work carried on at the Orthopedic Hospital-School for Crippled Children at Los Angeles. The institution is only four years old, yet it has enrolled for the current year 3,139 patients. Its aim is not only to restore as far as possible the physical functions lost through disease, but also to develop among the children the moral courage necessary to equip them for the battle of life. The society aims to provide suitable social contact and gives adequate instruction in vocations fitted to physically handicapped persons.

DANGEROUS OCCUPATIONS FOR MINORS. CHALLAUD, Rev. internat. de l'enf. **2**:797 (Sept.) 1926.

The author considers especially the moral environment of certain occupations not in themselves dangerous, such as dressmaking, lithography, the manufacture of perfumery, etc. The evil influences surrounding young persons, especially girls, engaged in the sale of liquor, is stressed. While it is difficult

to prohibit the employment of minors in these places, some system of regulation or inspection might be devised that would protect boys and girls from the moral contamination now manifest.

PROTECTION OF MOTHERS DURING PREGNANCY. DELA VILLA, Rev. internat. de l'enf. **2**:803 (Sept.) 1926.

Safety of the expectant mother should be taught in all schools for girls and in advanced classes for young women. To obtain maximum efficiency, this protection should be assumed by the government which could carry out suitable regulations through the various welfare associations. Maternity work may well begin with mother's clinics, with lectures by competent authorities and moving pictures. It can be reinforced by allowing free meals for pregnant women and, on occasion, by suitable grants from the state. Maternal insurance is recommended.

ADDITIONAL GERMAN ENACTMENTS FOR THE PROTECTION OF THE YOUNG. KOEHNE, Rev. internat. de l'enf. **2**:813 (Sept.) 1926.

Since the close of the war, many legislative reforms have been instituted, such as the protection of youth against the evils of alcoholism, the cinema, immoral literature and the sale of tobacco. Laws have been passed providing for equal care, morally, socially and physically, of legitimate and illegitimate children. Restrictive measures have been drafted to control the adoption of infants. All of these are actively enforced, and the author believes that much has been gained, if only in the renewed interest awakened toward child life.

AMESSE, Denver.

CONTRIBUTIONS TO VACCINE DIAGNOSIS. G. CASTORINA, Clin. pediat. **7**:372 (June) 1926.

Various vaccines were injected intradermally as a diagnostic test in many diseases. The dose for adults was 1 cc. and 0.5 cc. for children. The reactions were graded as weakly positive, positive, strongly positive and negative. The diagnosis were confirmed and controlled by clinical, bacteriologic and serologic observations.

In eighteen cases of whooping cough, ten in the catarrhal and eight in the convulsive stage, the reaction was weakly positive in five, positive in seven, strongly positive in four and negative in two.

In twelve cases of influenzal bronchopneumonia, there were eight positive reactions with the influenza vaccine; two weakly positive with pneumococcus vaccine and two positive with a combined influenza and pneumococcus vaccine. In one case of typhoid fever the vaccine diagnosis was strongly positive on the twelfth day, and the agglutination test made on the fifteenth day was positive in a dilution of 1:500.

In another case the vaccine diagnosis for typhoid fever was weakly positive, and for paratyphoid was strongly positive. The serologic test made at the same time was negative. When repeated on the fourteenth day it was positive for paratyphoid. Out of ten cases of metapneumonic pleurisy, a positive reaction was obtained in nine patients with pneumococcus vaccine and in one with streptococcus vaccine.

In three cases of influenzal meningitis, a positive reaction to influenza vaccine was obtained. In five cases of furunculosis there were three positive

reactions with the staphylococcus vaccine and two positive reactions with the streptococcus. In five cases of infantile gonococcal vulvovaginitis there were strongly positive reactions to a vaccine made from gonococci recovered from foci in the patients. The reactions to vaccines made from gonococci isolated from adults were poor. In one case of tuberculous pleurisy the response was negative to all vaccines used.

During an epidemic of measles, the author used various diagnostic vaccines during the prodromal and eruptive stages with negative results. This method of diagnosis is recommended especially to physicians who are not in close contact with laboratories.

ZAMBARANO, Northville, Mich.

ON THE PATHOGENESIS OF THE PYRAMIDAL CHEST. DOMENICO LARINI, Riv. di clin. pediat. **24**:677, 1926.

Altered development of the sternum, imperfect function of the diaphragm, emphysema from trouble in breathing and overactivity of the accessory muscles of respiration are the conditions necessary for development of the pyramidal chest.

HIGGINS, Cincinnati.

THE DIFFICULTY OF EDUCATING CHILDREN. CARL POTOTZKY, Ztschr. f. Kinderh. **41**:88, 1926.

It has been attempted to solve the problem of children difficult to educate by putting the purely exogenous factors in the foreground, such as milieu and personal experience, with emphasis on the sexual point of view. However, the picture is incomplete without the consideration of endogenous factors such as disturbance in the sphere of thought, volition and emotion. Children who are difficult to rear include, besides the idiot and imbecile, those with disturbances of perception, attention and memory, such as epileptic, mongolian, and schizophrenic disorders, and those who have had inflammatory processes in the cerebrum. Premature children often show disturbances of intelligence in later life but these are shown less often than disturbances of emotion and volition, which are made worse because these children are spoiled. Children who fly into a passion easily, are too shy or whine all the time, who have conflicts at school and social conflicts at the age of puberty belong to the class difficult to rear because of disturbances of volition. Disturbances of emotion are often bound up with disturbances of volition. Hysterical children belong to this class and also rough children who suffer not so much from a retardation of the ethical sense as from a lack of it. These are especially hard to educate.

The author believes that psychanalysis is not without danger and that emotions other than that of sex, such as fear, for instance, may retard children. The treatment must be individual, and all factors must be considered. It must be remembered that before exogenous factors can harm a child there must be an endogenous base. Emotionally emphasized experiences and injuries due to milieu will bring a retarding influence only to the psychopathologic child; that is, harmful conditions at home, such as unwise training, cannot long harm a robust child.

EMERSON, Boston.

# Society Transactions

## NORTHWESTERN PEDIATRIC SOCIETY

*Minneapolis, Oct. 15, 1926*

C. A. Stewart, M.D., *President, in the Chair*

The Development of the Paranasal Sinuses and Mastoid Cells. Presented by Dr. Richard E. Scammon.

The development of the paranasal sinuses begins in the middle third of prenatal life, but, with the exception of the maxillary sinus, they rarely develop beyond the stage of epithelial pockets before birth. At birth the maxillary sinus has already produced an elongated oval excavation in the medial wall of the maxilla. In general, the maxillary sinus proceeds first in postnatal growth, the ethmoidal sinuses come next, while the frontal and sphenoidal sinuses expand more slowly. The ethmoidal sinuses generally involve the bony wall of the nasal cavity in the first year, and the frontal and sphenoidal sinuses usually form excavations in their respective bones in the second or third years.

At birth, the cavity of the middle ear and the mastoid antrum have reached adult size, but the mastoid cells, when present, are represented only by epithelial buds or, at most, by one or two small chambers less than 5 mm. in diameter. The later development of these cells shows great individual variation, as does the mastoid process. The latter structure is generally present at the age of 1 year, but it usually does not extend below the inferior margin of the temporal bone before the age of 3. Rogers found the cells indicated by small pockets from the antrum at birth, and these appeared as distinct, flasklike cavities at 3 years. At 5 years, a large series of cells was present, their size being about half the average at maturity. During development, the mastoid cells first extend posteriorly and then downward with respect to the mastoid antrum.

Sinusitis in Children. Presented by Dr. John F. Curtin.

The author discusses the progress in diagnosis and treatment of sinusitis and compares the condition in a child with that in an adult. Obscurity of cause, symptoms and constitutional disorders are stressed. The aid of the roentgen-ray, the nasopharyngoscope and the exploratory needle puncture under the inferior turbinate are mentioned as diagnostic aids. Discussion of the acute and chronic forms was taken up with the treatment of each.

"At the beginning of an attack conservative intranasal treatment with astringent and cleansing solutions together with purgation and forced fluids will often bring the condition under control and effect a cure. Suction should also be used. In these cases a silver preparation was used together with a weak solution of cocaine epinephrine hydrochloride whenever it was considered necessary. Vaccines for a while was considered very useful in this class of cases, but experience has brought this treatment into disfavor.

"The tonsils and adenoids should be removed in all cases, for 70 per cent of the patients recover after this procedure. The other 30 per cent require, in addition to the adenoidectomy and tonsillectomy, some surgical treatment of

the antrum, and in most of the cases irrigation of the antrum under the inferior turbinate and enlarging the openings made by the trochar will effect a cure. Subsequently astringent solutions and suction should be used in these cases. Occasionally further irrigations are necessary, but one irrigation is usually sufficient. When the disease is so advanced as to involve the orbit or cheek, a most extensive operation is required. However, in these cases the greater part of the work should be done intranasally and not through the canine fossa because of the danger of destroying the teeth germs."

A short discussion on the diagnosis and treatment of mastoiditis in general was given in some detail.

THE DIAGNOSIS AND IMPORTANCE OF SINUSITIS AND MASTOIDITIS. Presented by DR. P. C. JEANS.

Any condition that may result from a focus of infection may result from paranasal sinusitis. In addition, numerous important symptoms and clinical conditions are more closely related to and even specifically dependent on sinusitis.

The influence of infection on the sugar tolerance in diabetes is well recognized. Many of the diabetic patients have been shown to have chronic sinusitis. Treatment of this infection has served to stabilize a previously unstable insulin requirement and in several instances has resulted in a considerable lowering of the necessary amount of insulin.

Many children have recurrences of chorea, rheumatic fever or endocarditis in spite of complete removal of tonsils and adenoids. In such children the author has nearly always found sinusitis present, often of marked severity. Treatment for sinusitis in these cases usually has resulted in the absence of further recurrence of rheumatic manifestations. In the instances in which the manifestations reappeared, recurrence of the sinusitis usually could be observed.

In the past, it has been customary to see chronic deforming arthritis continue to progress in spite of all treatment. In such cases the rhinologic examination was usually said to be negative. During the last two years, the author has seen approximately twelve patients whose arthritis could be classified under this heading. Sinus disease was invariably present, and the treatment of the sinusitis had resulted in complete relief from signs of activity in all instances. In only one, because of great periarticular thickening, did function remain materially impaired. In a few instances the rhinologist had been called in consultation as many as three times before he was willing to make a diagnosis of sinusitis. In these instances the inflammation was of a hyperplastic rather than of a suppurative type.

Sinusitis apparently has shared the responsibility with tonsillitis in several instances of acute hemorrhagic nephritis. A case was cited in which ethmoiditis seemed to be entirely responsible for chronic glomerular nephritis.

It is the presenter's opinion that sinusitis is the underlying cause of parenchymatous nephritis in all instances. A case presenting evidence of this relationship was cited.

In some conditions that are considered as cyclic vomiting, the symptoms seem to be due to sinusitis, since relief is obtained by eradication of the sinus disease.

The clinical picture described in the textbooks under cholera infantum or alimentary intoxication can be produced by either mastoiditis or sinusitis. These symptoms may be caused to disappear promptly by free drainage from the site of infection. Cases of cholera infantum in which upper respiratory infection was not present have not come to the author's attention. Cases were cited to illustrate this relationship.

From the pediatrician's standpoint, the diagnosis of sinus or mastoid disease is made chiefly on the basis of the clinical picture rather than from any local examination. This is particularly true when the clinical picture is as definite and distinctive as it is in cholera infantum. In other instances, all the pediatrician can determine is that there is an infection present whose localization is unknown and that by exclusion it probably is located in the sinuses or mastoids. For the successful working out of these diagnostic problems, it is essential that the pediatrician and otorhinologist work together in the closest cooperation and with entire confidence in each other. It is at times necessary for the pediatrician to insist on operative intervention when the otorhinologist cannot find sufficient anatomic evidence to warrant such a procedure.

DISCUSSION

Dr. E. J. Huenekens: When Dean and Byfield first published their monograph on sinuses I became interested in the subject. From my previous clinical experience, I felt that there must be some focus of infection in childhood other than tonsils and adenoids, and my subsequent experience with sinus work had been satisfactory. Besides the rheumatic cycle and nephritis mentioned by Jeans, drainage of the maxillary sinuses has proved particularly satisfactory in chronic or recurring pyelitis, in juvenile asthma (when the attacks accompany upper respiratory infections), in recurring bronchitis and in otitis. It has been difficult to secure the cooperation of rhinologists. I believe that the pediatrician, having studied the general condition of the child, has more knowledge of the likelihood of a focus of infection and should decide when operation is necessary rather than the rhinologist, who gets his evidence purely from a local condition.

The roentgen-ray diagnosis of sinusitis is not always satisfactory, some apparently negative sinuses showing pus, other apparently positive ones not yielding pus or bacteria.

Adenoidectomy should be performed in every case of washing of the sinus. In most of my cases that require tonsillectomy, I have the maxillary sinuses washed out as a matter of routine, thus removing all possible foci of infection at one sitting.

From Jeans' emphasis on ethmoid sinuses, I feel that I have been overlooking them as a probable focus of infection and in the future will have them more carefully investigated.

As to mastoiditis with alimentary intoxication, three such cases have been seen at the Minneapolis General Hospital. Two of the patients were operated on, but it was too late. In all three instances autopsy revealed thick pus in both mastoids, and in the future I shall look more carefully for both mastoiditis and sinusitis in the more severe alimentary intoxications.

Dr. C. A. Stewart: In a study of the maxillary sinuses of children the following experiences were encountered: When repeated roentgenograms of the sinuses were taken at intervals of several weeks, cloudiness of the maxillary sinus was seen to disappear in several cases without surgical intervention.

In a series of thirteen children who had bronchiactasis, an involvement of the maxillary sinuses was demonstrated. In twelve this was confirmed by roentgent ray and in eight by drainage. Sinus infections apparently occur in the majority of children who have this chronic pulmonary condition.

# Book Reviews

UNTERSUCHUNGEN UEBER DEN STOFFWECHSEL DES KINDES IM FIEBER. By PROFESSOR DR. W. BIRK. Price, 7 marks. Paper. Pp. 104, with nineteen illustrations. Berlin: S. Karger, 1926.

Birk studied the metabolism of eleven infants during their febrile period. The fever in some of them was due to vaccination and in others to measles or chickenpox. All the infants were normal in every other respect, and all of them were fed artificially.

The nitrogen metabolism showed marked changes during the incubation period, the active febrile period and the postfebrile period. The author believes that the nitrogen balance is even a finer indication of the child's condition than the temperature and weight curve. In most cases there was a loss of nitrogen during the febrile period. In the prefebrile period, however, there was an increase in the nitrogen retention.

The author does not believe that the loss in nitrogen is due to toxigenic decomposition of protein, as has been held for many years. He believes that it is all due to a disturbance of the central regulation of protein metabolism. The loss in nitrogen during the febrile period depended on the severity of the infection and on the duration and height of the fever. With a slight rise in temperature, there was only a lessening of nitrogen retention, but with a higher rise in temperature the nitrogen balance became negative. He found no parallelism of loss of nitrogen to the weight curve. He thinks that the weight curve has nothing to do with the protein metabolism but has mostly to do with the mineral substances. The nitrogen loss may be explained, he says, by the relative undernourishment of the child during the febrile period, which is apparent even if the child takes as much food as usual.

During the postfebrile period, there was no great retention of nitrogen. At least, the retention was lower than it was during the period of health. The author therefore believes that the term reconvalescence may be applied to this period, as the child is not yet normal but is gradually approaching such a state. It is hard to tell whether the loss of nitrogen in the first day of convalescence is due to central disturbances, regulatory disturbances or to the secretion of a toxic protoplasm or to a loss of a part of the protein which was burnt up during the febrile period. One thing is certain, that the body shows little tendency to repair the protein loss during convalescence.

Ten cases were studied for chloride retention. In mild infections, the chloride metabolism was uninfluenced. In several infections, the chloride retention in some cases was noticeable even in the incubation period, and sometimes there was a marked prefebrile excretion of chlorides. There was no constant relation between the chloride retention and the increase in weight.

The calcium, as a rule, was diminished in the blood during the febrile period, the excretion being through the stool. The changes were already marked in the incubation period and could be demonstrated even after the disappearance of the fever.

The excretion of acid phosphates usually was increased during the febrile period. In some cases, however, there was a retention of it. The excretion

was mainly by way of the kidneys and to a lesser degree by way of the intestinal tract. The increase was already noticeable in the incubation period.

The metabolism of alkalis in general is inconstant. In some cases there was an increase in excretion, and in other cases there was a retention.

NOURRISSONS ENFANTS. Par G. BLECHMANN. Price, 18 francs. Pp. 387. Paris: Gaston Doin, 1926.

This little book on the diseases of infancy covers the subject briefly but thoroughly. The author's contraindications to breast feeding seem rational, and are those generally accepted by most pediatricians. Some of these may be enumerated: pulmonary tuberculosis; cardiac disease without compensation; nephritis without edema; serious diseases of the liver, stomach and nervous system. These contraindications differ considerably from those described by certain American pediatricians of only a few years ago, who advised that there were no contraindications to breast feeding except tuberculosis in the mother. It seems that the author has taken a sensible attitude on contraindications to breast feeding.

Other diseases enumerated are grip, scarlet fever, measles and typhoid fever, which depend on the mother's ability to nurse the baby under these conditions.

The author mentions a number of articles of food as being bad for the milk; they are onions, asparagus, cauliflower, rhubarb, shellfish, alcohol, etc. I believe that most pediatricians feel that it is not practical to advise a mother, particularly one who is nervous, in detail as to what she should eat while nursing her baby other than the general advice that she eat the same simple, plain wholesome food that she had been in the habit of eating before the baby came.

The care of the breast before the arrival of the baby is briefly touched on in a satisfactory manner, as well as the treatment of engorged and abscessed breasts. The description of the treatment of mixed feedings is rational, and the reviewer believes is in general use. These chapters, while useful, contain nothing new.

Chapters 2 and 3 are devoted to the modification of milk mixtures, the use of condensed milk, malted milk, modified milk, albumin milk and the preparation of simple milk modifiers and of vegetables and cereals. Chapter 4 contains a series of diets for children up to 2 years of age.

There is nothing new in these diet lists, which conform in general with those that most pediatricians use with individual variations. Certain alimentary difficulties, such as malformations and pathologic conditions of the new-born, all of which are included in most of the recent textbooks on infancy and childhood, are described.

Some of the author's prescriptions as well as some by Professor Marfan, Netter and others, are given. The remainder of the book is devoted to other common disorders of infancy and early childhood, together with prescriptions and treatments that the author has found useful. The book is completely indexed, and while in general it contains nothing new to pediatricians, it would be of use to any physician who treats infants.

DAS WACHSTUM DAS KINDES. By PROF. DR. EUGEN SCHLESINGER. Price. 6 gold marks. Paper. Pp. 128. Berlin: Julius Springer, 1926.

The author gives an historical résumé of the study of growth and development. He divides the history of the subject into two main periods: the one of mass investigation in which many children belonging to different groups

were measured and tables computed from the average results, and the new period in which the growth of the same individual is studied. The author points out the inaccuracies and difficulties accompanying the study of growth in children when the measurement is taken by more than one person. He also points out the difference in the weight of the child at various periods of the day, the difference amounting sometimes to between 150 and 500 Gm. in infants and 700 Gm. in older children. The author also speaks of the inaccuracy of weighing children with their clothes on. Some of his results are as follows:

The difference in growth in the two sexes is noticeable during intra-uterine life. The absolute length and weight of boys are greater than the corresponding weight and length of girls, but the relative figures in the percentages in relation to body length are smaller.

From the standpoint of growth, the author divides the year into three periods: the first third from December to April, in which there is a medium gain in length and weight; the second third from April to September, in which there is an intensive increase in length, and the third period which runs from September to December. In the last period there is the smallest increase in length and the largest increase in height. The loss in weight which is noticeable the early part of the summer has nothing to do with attendance at school, because it is noticeable also in children who do not attend school. The periodicity of the weight curve during the various periods of the year is noticeable even in infants.

The thymus that is well developed in the period of the most active growth and becomes atrophied at the time growth stops is the central organ of growth, and also the central organ of vitamin metabolism.

In hyperplasia of the thyroid gland in childhood, the growth is also increased. Hypopituitary disturbance of growth, whether it is a decrease or an increase, is noticeable only in later childhood.

THE FINER DIAGNOSES OF ACUTE BRAIN INVOLVEMENTS. J. VICTOR HABERMAN, Monograph, M. J. & Record, 1925, vol. 121.

In this short monograph, an attempt is made to offer a guide for more exact differentiation of the many pathologic processes which produce the more or less uniform picture of acute involvement of the brain, primarily affecting the pallium. Emphasis is placed on the determination of the nature of the disease process rather than on its localization.

Of the infectious conditions, Heine-Medin disease, epidemic encephalitis, influenzal encephalitis, together with nonspecific meningo-encephalitis, secondary hemorrhagic encephalitis, meningitis serosa, and purulent and tuberculous meningitis receive the most attention. Syphilis of the brain is included in so far as it may be acute or related to other acute conditions; the differentiation of one type from another is based largely on spinal fluid observations. In considering brain trauma, the author gives much space to the delayed episodes; late bleeding or edema, posttraumatic epilepsy, neuroses, psychoses and disturbances of behavior. The acute vascular accidents, cerebral hemorrhage (arteriosclerotic), thrombosis and embolism, together with the bleeding of a hemorrhagic diathesis and in toxic conditions are, of course, presented. Cerebral thrombosis other than syphilitic is regarded as infrequent.

The paper is a distillate of an extensive literature, and a fairly copious bibliography is appended.

KOZENTRATIONSGYMNASTIC FÜR ZERSTREUTE UND NERVOESE KINDER. By DR. MED. CARL POTOTZKY. Price, 3 marks. Pp. 80, with thirty-five illustrations. Leipzig: George Thieme, 1926.

This monograph can be recommended to pediatricians, neurologists, psychiatrists, physical instructors, teachers and parents for three reasons: 1. It is brief and precise. 2. It presents a practical, specific, dynamic form of therapy. 3. It covers a much neglected and important method of overcoming certain deficiencies in children. The author has had a great deal of experience in the diagnosis and management of subefficient children. In this work he is especially concerned with children who cannot concentrate, who are restless and whose inhibition and coordination are poor. He demonstrates, through vivid illustrations, thirty-four specific exercises whose purpose is the education of children in balance of the nerves and muscles. He suggests those forms of exercise which imitate common daily activities of the child, such as brushing the teeth, washing the face, dressing, running and playing games.

The reviewer, although himself lacking personal experience with these particular exercises, believes that they have a logical place in the management of so-called nervous children.